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(54) Urea derivatives and their use as acat inhibitors

Urea-Derivate und ihre Verwendung als ACAT-hemmenden Verbindungen

Dérivés d'urea et leur utilisation comme inhibiteurs d'ACAT

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(73) Proprietor: **NISSHIN FLOUR MILLING CO., LTD.**
Chuo-ku, Tokyo (JP)

(72) Inventors:
- **Sueda, Noriyoshi,**
  c/o Nisshin Flour Milling Co.
  Ohimachi, Iruma-gun, Saitama-ken (JP)
- **Yamada, Kazuhiko,**
  c/o Nisshin Flour Milling Co.
  Ohimachi, Iruma-gun, Saitama-ken (JP)
- **Yanai, Makoto,**
  c/o Nisshin Flour Milling Co.
  Ohimachi, Iruma-gun, Saitama-ken (JP)
- **Miura, Katsutoshi,**
  c/o Nisshin Flour Milling Co.
  Ohimachi, Iruma-gun, Saitama-ken (JP)
- **Horigome, Masato,**
  c/o Nisshin Flour Milling Co.
  Ohimachi, Iruma-gun, Saitama-ken (JP)
- **Oshida, Norio,**
  c/o Nisshin Flour Milling Co.
  Ohimachi, Iruma-gun, Saitama-ken (JP)
- **Hiramoto, Shigeru,**
  c/o Nisshin Flour Milling Co.
  Ohimachi, Iruma-gun, Saitama-ken (JP)
- **Katsuyama, Koichi,**
  c/o Nisshin Flour Milling Co.
  Ohimachi, Iruma-gun, Saitama-ken (JP)
- **Nakata, Fumihisa,**
  c/o Nisshin Flour Milling Co.
  Ohimachi, Iruma-gun, Saitama-ken (JP)
- **Kinoshita, Nobuhiro,**
  c/o Nisshin Flour Milling Co.
  Ohimachi, Iruma-gun, Saitama-ken (JP)
- **Tsukada, Yoko,**
  c/o Nisshin Flour Milling Co.
  Ohimachi, Iruma-gun, Saitama-ken (JP)

(74) Representative: **Marshall, Monica Anne**
J.A. KEMP & CO.
14 South Square
Gray's Inn
London WC1R 5LX (GB)

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Description

FIELD OF THE INVENTION

This invention relates to new urea derivatives, processes for their preparation and their use in medicine. More particularly, the invention relates to compounds having an inhibitory activity against an acyl coenzyme A cholesterol acyltransferase (called hereafter ACAT) and having a protective ability against an oxidative modification of low density lipoprotein (called hereafter LDL).

BACKGROUND OF THE INVENTION

In recent years, interest has been directed to the relationship between increase in the level of cholesterol in the serum and human health. It has been pointed out that the level of cholesterol in the serum is associated with the amount of cholesterol deposited in the blood vessel system and the deposition of cholesterol in the blood vessel system brings about e.g. coronary artery lesion, which is responsible for ischemic heart disease.

Drugs for reducing the level of cholesterol in the serum have been developed. These drugs, however, were effective in controlling blood cholesterol to an appropriate level, but ineffective in inhibiting absorption of cholesterol from the digestive tracts and deposition of cholesterol on the wall of blood vessels.

ACAT is an enzyme that catalyzes the synthesis of cholesteryl esters from acyl coenzyme A and cholesterol and plays an important role in cholesterol metabolism and its absorption from the digestive tracts. It is believed that ACAT occurs in the site of mucosa cells of intestinal tracts and is active in esterification and incorporation of cholesterol derived from the diet. On the other hand, the cholesterol deposited on the wall of blood vessels is the esterified cholesterol. The cholesterol accumulated in the foam cells which plays in important role in the formation of atherosclerosis lesion is also esterified cholesterol. The enzyme that catalyzes the esterification of cholesterol in these sites is also ACAT.

Accordingly, the inhibition of ACAT activity can result in inhibiting the incorporation in vivo of cholesterol derived from the diet and further the formation of cholesteryl ester in specified cell sites.

Compounds having an ACAT inhibitory activity are disclosed in EP 0450660 A1 and EP 0477778 A2. However, those known compounds have only an ACAT inhibitory activity and give no effect on the oxidative modification of LDL causing the foam cell transformation of macrophage which is an important phenomenon for the formation of atherosclerosis lesion.

The foam cells which play an important role in the formation of atherosclerosis lesion are products of uptake of oxidatively modified LDL into macrophage which results in the foam cell transformation of the macrophage. It is reported by Diane W. Morel et al. (Atheroma, Vol. 4, pages 357-364, 1984) that, the oxidatively modified LDL causes foam cell transformation of macrophage and plays an important role in the formation of atherosclerosis lesion. A report of TORU KITA et al. (Proc. Natl. Acad. Sci. USA, Vol. 84, pages 5928-5931, 1987) demonstrates that prevention of the oxidative modification of LDL induces regression of the atherosclerosis lesion. Therefore, inhibition of the oxidative modification of LDL, in addition to the above-mentioned ACAT inhibitory activity, is very important in preventing the formation and progression as well as inducing regression of atherosclerosis lesion.

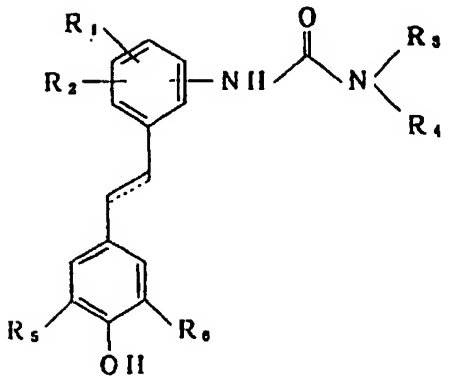
Under such circumstances, it has been desired to develop compounds having an ACAT inhibitory activity and capable of inhibiting an oxidative modification of LDL or the like, since such compounds may decrease the serum cholesterol level and inhibit the oxidative modification of LDL cholesterol deposited on the blood vessel or tissue, thus being effective for inhibiting the formation and progression of atherosclerosis lesions and inducing its regression.

EP-A-0 527 458 discloses certain new 3,5-di-tert-butyl-4-hydroxyphenyl derivatives which are described as having antioxidant activity and being capable of inhibiting ACAT-dependent esterification. The compounds disclosed are described as being useful as medicaments, especially as anti-atherosclerotics.

DETAILED DESCRIPTION OF THE INVENTION

We have now found new urea derivatives which exhibit both an ACAT inhibitory activity and an antioxidative activity. The urea derivatives of the present invention possess an ACAT inhibitory activity, thereby inhibiting absorption of cholesterol from the intestinal tracts, lowering blood cholesterol level and inhibiting accumulation of cholesteryl esters in the wall of blood vessels, atheroma and macrophage, and simultaneously an antioxidative activity i.e. a protective activity against the oxidative modification of LDL which participates in foam cell transformation of macrophage thereby effectively inhibiting the formation and progression of atherosclerosis lesion and inducing its regression.

According to one aspect of the present invention, there is provided a compound of formula (I) and pharmaceutically acceptable salts thereof, which exhibits both an ACAT inhibitory activity and an antioxidative activity.



(I)

in which:

R_1 and R_2, which may be the same or different, each represents

a hydrogen atom,
a halogen atom,
a straight or branched $(C_1\text{-}C_6)$alkyl group or
a straight or branched $(C_1\text{-}C_6)$alkoxy group,

R_3 and R_4, which may be the same or different, each represents

a hydrogen atom,

a straight or branched $(C_1\text{-}C_{12})$alkyl group,

a straight or branched $(C_2\text{-}C_{20})$alkenyl group,

a $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl group,

a $(C_1\text{-}C_6)$alkoxycarbonyl$(C_1\text{-}C_9)$alkyl group,

a benzyloxycarbonyl$(C_1\text{-}C_6)$alkyl group in which the alkyl moiety is optionally substituted by phenyl,

a N,N-di$(C_1\text{-}C_6)$alkylamino$(C_1\text{-}C_6)$alkyl group,

a N-$(C_1\text{-}C_6)$alkyl-N-benzylamino$(C_1\text{-}C_6)$alkyl group,

a $(C_1\text{-}C_6)$alkylthio$(C_1\text{-}C_6)$alkyl group,

an oxo$(C_1\text{-}C_9)$alkyl group,

a hydroxy$(C_1\text{-}C_6)$alkyl group,

a dihydroxy$(C_1\text{-}C_6)$alkyl group,

a cyclo$(C_3\text{-}C_{15})$alkyl group,

a cyclo$(C_3\text{-}C_8)$alkyl$(C_1\text{-}C_6)$alkyl group,

a dicyclo$(C_3\text{-}C_9)$alkyl$(C_1\text{-}C_6)$alkyl group,

a bicyclo(C_6-C_9)alkyl group,

a tricyclo(C_9-C_{12})alkyl group,
in which in all cases the cycloalkyl group or the cycloalkyl moiety is optionally substituted by one or two substituents selected from the group consisting of (C_1-C_6)alkyl, hydroxy, amino, acetoxy, acetamido, phenyl, benzyloxy, dimethylaminophenyl, and methylenedioxyphenyl, which may be further fused with a benzene ring,

an aryl group,

an aryl(C_1-C_6)alkyl group,

a diaryl(C_1-C_6)alkyl group,
in which in all cases the aryl group or the aryl moiety is optionally substituted by one, two or three substituents selected from the group consisting of (C_1-C_6)alkyl, (C_1-C_6)alkyloxy, halogen, nitro, hydroxy, amino, dimethylamino, methylenedioxy, and pyrrolidinyl,

a heterocyclic group or

a heterocyclic group attached to a (C_1-C_6)alkylene chain,
in which in all cases the heterocyclic group represents a saturated or unsaturated, 5 to 8 membered ring monocyclic or bicyclic, heterocyclic group containing 1 to 3 heteroatoms selected from the group consisting of S, O and N, and the heterocyclic group is optionally substituted by one or two substituents selected from the group consisting of acetyl, hydroxy, (C_1-C_9)alkyl, (C_1-C_9)alkyloxy, cyclo(C_3-C_8)alkyl, cyclo(C_3-C_8)alkyl(C_3-C_{10})alkyl, pyridyl(C_1-C_6)alkyl, phenyl, phenyl(C_1-C_6)alkyl, diphenyl(C_1-C_6)alkyl, and phenylpiperazinyl, the phenyl group or the phenyl moiety being optionally substituted by one or two substituents selected from the group consisting of halogen, hydroxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, cyano, diethylamino and trifluoromethyl, which may be further fused with a benzene ring,

and further R_3 and R_4, together with the nitrogen atom to which they are attached, may form a saturated or unsaturated heterocyclic group,
in which the heterocyclic group represents a 5 to 8 membered ring monocyclic or bicyclic, heterocyclic group or a group derived from a heterocyclic spiro compound, which may contain one or two heteroatoms selected from the group consisting of S, O or N, the heterocyclic group being optionally substituted by one or two substituents selected from the group consisting of (C_1-C_6)alkyl, hydroxy, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, acetoxy(C_1-C_6)alkyl, (C_1-C_9)alkylcarbonyl, (C_1-C_6)alkoxycarbonyl, amino, tosyl, phenyl, halogenophenyl, (C_1-C_6)alkoxyphenyl, phenyl(C_1-C_6)alkyl, benzyloxy, benzyloxy(C_1-C_6)alkyl, tolyl, xylyl, benzoyl, methylenedioxyphenyl(C_1-C_6)alkyl, pyridyl, pyridylcarbonyl, piperidyl, pyrrolidinyl(C_1-C_6)alkyl and pyrrolidinylcarbonyl(C_1-C_6)alkyl, which may be further fused with a benzene ring,
in which in all cases the alkyl and alkoxy moieties may be either straight or branched,
with the proviso that both R_3 and R_4 do not represent a hydrogen atom at the same time;
R_5 and R_6, which may be the same or different, each represents a straight or branched (C_1-C_6)alkyl group; and the line

represents $-CH_2CH_2-$ or $-CH=CH-$.

Referring to R_1 and R_2 in formula (I), the halogen atom includes fluorine, chlorine, bromine and iodine, the (C_1-C_6)alkoxy group includes e.g. methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, sec-butoxy, tert-butoxy, pentyloxy and hexyloxy, and the (C_1-C_6)alkyl group includes e.g. methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, pentyl and hexyl.

Referring to R_3 and R_4 in formula (I), the (C_1-C_{12})alkyl group includes e.g. methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, isopentyl, neopentyl, hexyl, isohexyl, heptyl, octyl, trimethylpentyl, 2,4,4-trimethyl-2-pentyl, nonyl, decyl and dodecyl. The (C_2-C_{20})alkenyl group includes e.g. vinyl, allyl, isopropenyl, 2-butenyl, 2-pentenyl, 4-pentenyl, 3-hexenyl, 5-hexenyl, 4-octenyl, 7-octenyl, 7-decenyl, 3,7-dimethyl-2,6-octadienyl, 10-tetradecenyl, 8-heptadecenyl, 8-octadecenyl and 4,7,10,13,16-nonadecapentaenyl. The (C_1-C_6)alkoxy(C_1-C_6)alkyl group includes e.g.

2-methoxyethyl, 4-methoxybutyl, 2-methoxybutyl, 6-methoxyhexyl, ethoxymethyl, 3-ethoxypropyl, 2-propoxyethyl, 5-propoxypentyl, isopropoxymethyl, butoxymethyl, 2-isobutoxyethyl, sec-butoxymethyl, tert-butoxymethyl, pentyloxymethyl, 2-pentyloxyethyl and hexyloxymethyl.

The (C_1-C_6)alkoxycarbonyl(C_1-C_9)alkyl group includes e.g. 2-(methoxycarbonyl)ethyl, 7-(methoxycarbonyl)heptyl, 2-(ethoxycarbonyl)ethyl, 4-(ethoxycarbonyl)butyl, propoxycarbonylmethyl, 3-(propoxycarbonyl)butyl, isopropoxycarbonylmethyl, butoxycarbonylmethyl, 1-(butoxycarbonyl)ethyl, 2-(isobutoxycarbonyl)ethyl, sec-butoxycarbonylmethyl, 2-(tert-butoxycarbonyl)ethyl, pentyloxycarbonylmethyl and 2-(hexyloxycarbonyl)ethyl, α-(methoxycarbonyl)benzyl, α-(ethoxycarbonyl)benzyl.

The benzyloxycarbonyl(C_1-C_6)alkyl group includes benzyloxycarbonylmethyl, 2-(benzyloxycarbonyl)ethyl, 6-(benzyloxycarbonyl)hexyl, 4-(benzyloxycarbonyl)butyl and α-(benzyloxycarbonyl)benzyl.

The N,N-di(C_1-C_6)alkylamino(C_1-C_6)alkyl group includes e.g. 2-(N,N-dimethylamino)ethyl, 4-(N,N-dimethylamino)butyl, 2-(N,N-diethylamino)ethyl, 3-(N,N-diethylamino)propyl, N,N-diisopropylaminomethyl, N,N-dibutylaminomethyl, 2-(N,N-dibutylamino)ethyl, 2-(N,N-diisobutylamino)ethyl, N,N-dipentylaminomethyl, 2-(N,N-dihexylamino)ethyl and N,N-diisohexylaminomethyl.

The N-(C_1-C_6)alkyl-N-benzylamino(C_1-C_6)alkyl includes e.g. 2-(N-benzyl-N-methylamino)ethyl, 2-(N-benzyl-N-ethylamino)ethyl, 4-(N-benzyl-N-methylamino)butyl, 2-(N-benzyl-N-ethylamino)ethyl and 3-(N-benzyl-N-ethylamino)propyl.

The (C_1-C_6)alkylthio(C_1-C_6)alkyl group includes e.g. 2-(methylthio)ethyl, 2-(ethylthio)ethyl, propylthiomethyl, 2-(isopropylthio)ethyl, 1-(butylthio)ethyl, isobutylthiomethyl, tert-butylthiomethyl, pentylthiomethyl and hexylthiomethyl.

The oxo(C_1-C_9)alkyl group includes e.g. 2-oxopropyl, 2-oxobutyl, 4-oxopentyl, 6-oxoheptyl and 2-oxooctyl.

The hydroxy(C_1-C_6)alkyl group includes e.g. 2-hydroxyethyl, 2-hydroxypropyl, 3-hydroxypropyl, 3-hydroxybutyl and 6-hydroxyhexyl.

The dihydroxy(C_1-C_6)alkyl group includes e.g. 2,3-dihydroxypropyl, 4,5-dihydroxypentyl, 1,5-dihydroxy-3-pentyl, 2-ethyl-1,3-dihydroxy-2-propyl, and 2,4-dihydroxy-3-methylpentyl.

The cyclo(C_3-C_{15})alkyl group includes e.g. cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclodecyl, cyclododecyl, 1-phenylcyclopentyl, 4-(benzyloxy)cyclohexyl, 4-aminocyclohexyl, 4-acetamidocyclohexyl, 4-hydroxycyclohexyl, 4-acetoxycyclohexyl, 4-tert-butylcyclohexyl, 2,3-dimethylcyclohexyl, 1,2,3,4-tetrahydronaphthyl, cyclododecyl and benzyloxycyclohexyl.

The cyclo(C_3-C_8)alkyl(C_1-C_8)alkyl group includes e.g. cyclopropylmethyl, 2-cyclobutylethyl, 2-cycloheptylethyl, cyclohexylmethyl, 3-cyclohexylpropyl, 4-cyclohexylbutyl, cyclooctylmethyl, 5-cyclooctylpentyl, 1-(4-dimethylaminophenyl)cyclopentylmethyl and 1-(3,4-methylenedioxyphenyl)cyclopentylmethyl.

The dicyclo(C_3-C_9)alkyl(C_1-C_6)alkyl group includes e.g. dicyclohexylmethyl, 2,2-dicyclohexylethyl and 3,3-dicyclohexylpropyl.

The bicyclo(C_6-C_9)alkyl group includes e.g. bicyclo[3.3.0]-2-octyl, bicyclo[3.3.1]-2-nonyl and bicyclo[3.2.1]-2-octyl.

The tricyclo(C_9-C_{12})alkyl group includes e.g. tricyclo[5.2.1.$0^{2,6}$]decyl and tricyclo[3.3.1.$1^{3,7}$]decyl.

The aryl group includes e.g. phenyl, 1-naphthyl, 2-naphthyl, 3-naphthyl, 4-methylphenyl, 2,6-diisopropylphenyl, 3,5-di-tert-butyl-4-hydroxyphenyl, 2-methoxyphenyl, 4-hexyloxyphenyl, 4-fluorophenyl, 2-nitrophenyl, 4-chloronaphthyl, 3-amino-2-naphthyl, 5-hydroxynaphthyl, 5-methoxynaphthyl and anthryl.

The aryl(C_1-C_6)alkyl group includes e.g. benzyl, phenethyl, α-methylbenzyl, 3-phenylpropyl, 4-phenylbutyl, 9-anthrylmethyl, 4-ethylbenzyl, 4-ethoxybenzyl, 4-fluorobenzyl, 3,4-methylenedioxybenzyl, 3,4,5-trimethoxybenzyl, 4-methylphenethyl, 2-methoxyphenethyl, 4-methoxyphenethyl, 3,4-dimethoxyphenethyl, 3-chlorophenethyl, 4-chlorophenethyl, 4-fluorophenethyl, 4-nitrophenethyl, 3,4,5-trimethoxyphenethyl, 4-nitrophenylbutyl, 1-(4-fluorophenyl)-2-methylpropyl, 3-(3,4-dichlorophenyl)propyl, 4-dimethylaminophenethyl, 2-(3,4-dichlorophenyl)-2-propyl, 2-(3,4-dichlorophenyl)-2-methylpropyl, 2-(2-fluorophenyl)-2-methylpropyl, 2-(3-fluorophenyl)-2-methylpropyl, 2-(4-fluorophenyl)-2-methylpropyl and 2-[4-(1-pyrrolidinyl)phenyl]-2-methylpropyl.

The diaryl(C_1-C_6)alkyl group includes e.g. diphenylmethyl, 1,2-diphenylethyl, 2,2-diphenylethyl, 4,4-diphenylbutyl and 6,6-diphenylhexyl.

The monocyclic, heterocyclic group includes e.g. 3-furyl, 2-thienyl, 3-pyrrolyl, 2-pyrrolidinyl, 2H-pyran-3-yl, 2-pyridyl, 4-piperidyl, 3-morpholinyl, 2-piperazinyl, 1-methyl-4-piperidyl, 1-benzyl-4-piperidyl, 1-methyl-3-piperidyl, 1-(2,4-difluorobenzyl)-4-piperidyl, 1-(3,4-difluorobenzyl)-4-piperidyl, 1-(3,5-difluorobenzyl)-4-piperidyl, 1-[2,4-bis(trifluoromethyl)benzyl]-4-piperidyl, 1-(4-methoxybenzyl)-4-piperidyl, 1-phenethyl-4-piperidyl, 1-(2-fluorobenzyl)-4-piperidyl, 1-(3-fluorobenzyl)-4-piperidyl, 1-(4-fluorobenzyl)-4-piperidyl, 1-(4-chlorobenzyl)-4-piperidyl, 1-(4-cyanobenzyl)-4-piperidyl, 1-(2-pyridylmethyl)-4-piperidyl, 1-(3-pyridylmethyl)-4-piperidyl, 1-(4-pyridylmethyl)-4-piperidyl, 1-[4-(N,N-diethylamino)benzyl]-4-piperidyl, 1-[bis(4-fluorophenyl)methyl]-4-piperidyl, 1-(4-fluorophenethyl)-4-piperidyl, 1-(2,4-dimethylbenzyl)-4-piperidyl, 1-acetyl-4-piperidyl, 1-(4-hydroxybenzyl)-4-piperidyl, 1-(3,4-dihydroxybenzyl)-4-piperidyl, 1-ethyl-4-piperidyl, 1-neopentyl-4-piperidyl, 1-cyclohexyl-4-piperidyl, 1-heptyl-4-piperidyl, 1-(2-propyl)-4-piperidyl, 1-benzyl-3-piperidyl, 2-phenyl-3-piperidyl, 1-cyclohexylmethyl-3-piperidyl, 1-benzyl-3-pyrrolidinyl, 2-methoxy-5-pyridyl, 2-(4-phenyl-1-piperazinyl)-5-pyridyl and 5,6-dimethyl-1,2,4-triazin-3-yl.

The bicyclic, heterocyclic group includes e.g. 3-indolyl, 5-indazolyl, 2-quinolyl, 5-isoquinolyl, 2,4-dimethyl-1,8-naph-

thyridin-7-yl, 3,9-dimethyl-3,9-diazabicyclo[3.3.1]-7-nonyl, 9-methyl-3-oxa-9-azabicyclo[3.3.1]-7-nonyl, 9-(4-fluorobenzyl)-3-oxa-9-azabicyclo[3.3.1]-7-nonyl, 9-methyl-3-thia-9-azabicyclo[3.3.1]-7-nonyl, 8-methyl-8-azabicyclo[3.2.1]-3-octyl and 1-azabicyclo[2.2.2]-3-octyl.

The heterocyclic group attached to an alkylene chain may be the above-mentioned monocyclic or bicyclic heterocyclic group attached to an alkylene chain, which includes e.g. 3-furylmethyl, 3-(2-thienyl)propyl, 2-(3-indolyl)ethyl, 2-(3-pyrrolyl)ethyl, 2-pyrrolidinylmethyl, 2-pyridylmethyl, 3-pyridylmethyl, 4-pyridylmethyl, 2-(2-pyridyl)ethyl, 2-(4-piperidyl)ethyl, 3-(3-morpholinyl)propyl, 3-indolylmethyl, 2-(5-indazolyl)ethyl, 2-quinolylmethyl, 3-(1-imidazolyl)propyl, 2-morpholinoethyl, 3-morpholinopropyl, 3-(2-methylpiperidyl)propyl, 2-(1-pyrrolidinyl)ethyl, [4-(4-fluorobenzyl)-3-morpholinyl]methyl and (1-benzyl-4-hydroxy-4-piperidyl)methyl.

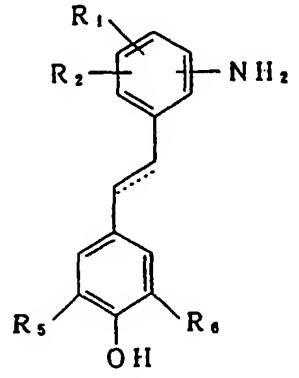
When R_3 and R_4 in formula (I), together with the nitrogen atom to which they are attached form the heterocyclic ring, the monocyclic, heterocyclic group includes e.g. pyrrolidinyl, 2,5-dimethyl-1-pyrrolidinyl, 3-hydroxy-1-pyrrolidinyl, 2-hydroxymethyl-1-pyrrolidinyl, 2-hydroxyethyl-1-pyrrolidinyl, 2-methoxymethyl-1-pyrrolidinyl, 2-(1-pyrrolidinylmethyl)pyrrolidinyl, 3-pyrrolin-1-yl, 2,5-dimethyl-3-pyrrolin-1-yl, piperidino, 2-methylpiperidino, 2-ethylpiperidino, 3-methylpiperidino, 4-methylpiperidino, 4-piperidinopiperidino, 3,3-dimethylpiperidino, 2,6-dimethylpiperidino, 3,5-dimethylpiperidino, 2,4-dimethylpiperidino, 2-(hydroxymethyl)piperidino, 2-(2-hydroxyethyl)piperidino, 2-(2-acetoxyethyl)piperidino, 3-hydroxypiperidino, 4-hydroxypiperidino, 4-oxopiperidino, 4-aminopiperidino, 4-benzylpiperidino, 2-[2-(benzyloxy)ethyl]piperidino, 3-(benzyloxy)piperidino, 1,2,3,6-tetrahydropyridyl, perhydroazepinyl, perhydroazocinyl, piperazinyl, 4-methyl-1-piperazinyl, 3-methyl-1-piperazinyl, 3,5-dimethyl-1-piperazinyl, 2,5-dimethyl-1-piperazinyl, 4-(2-hydroxyethyl)-1-piperazinyl, 4-pentanoyl-1-piperazinyl, 4-acetyl-1-piperazinyl, 4-p-toluenesulfonyl-1-piperazinyl, 4-benzyl-1-piperazinyl, 4-(3,4-methylenedioxybenzyl)-1-piperazinyl, 4-(2-pyridyl)-1-piperazinyl, 4-nicotinoyl-1-piperazinyl, 4-(1-pyrrolidinylcarbonylmethyl)-1-piperazinyl, 4-benzyl-1-piperidyl, 4-phenyl-1-piperidyl, 4-phenyl-1,2,3,6-tetrahydropyridyl, 4-phenyl-1-piperazinyl, 4-benzyl-1-piperazinyl, 4-(o-tolyl)-1-piperazinyl, 4-(2-fluorophenyl)-1-piperazinyl, 4-(2,3-xylyl)-1-piperazinyl, 4-(2-chlorophenyl)-1-piperazinyl, 4-(2-methoxyphenyl)-1-piperazinyl, 4-(2-ethoxyphenyl)-1-piperazinyl, 4-(m-tolyl)-1-piperazinyl, 4-(3,4-difluorophenyl)-1-piperazinyl, 4-(4-chlorophenyl)-1-piperazinyl, 4-(3,4-dimethoxyphenyl)-1-piperazinyl, homopiperazinyl, morpholino, 2,6-dimethylmorpholino, thiazolidinyl, thiomorpholino, pyrrolyl, 2-ethyl-1-pyrrolyl, 2,5-dimethyl-1-pyrrolyl, pyrazolyl, 3-methyl-1-pyrazolyl, 4-methyl-1-pyrazolyl, imidazolyl, 4-methyl-1-imidazolyl, 4-phenyl-1-imidazolyl, 1H-1,2,3-triazol-1-yl, 1,2,4-triazol-1-yl, imidazolidinyl, 2-imidazolin-1-yl, pyrazolidinyl and 2-pyrazolin-1-yl.

The bicyclic, heterocyclic group includes e.g. 4,5,6,7-tetrahydroindol-1-yl, 1,5,6,7-tetrahydro-4-oxoindol-1-yl, indolinyl, isoindolinyl, perhydroindol-1-yl, decahydroquinolinyl, perhydroisoquinolin-2-yl, 1,2,3,4-tetrahydrocarbazol-1-yl, 1,2,3,4-tetrahydroquinolin-1-yl, 1,2,3,4-tetrahydroisoquinolin-1-yl, 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-yl, 5H-dibenz[b,f]azepin-5-yl, 10,11-dihydro-5H-dibenz[b,f]azepin-5-yl, 3-azabicyclo[3.2.2]nonan-3-yl, 3-methyl-3,9-diazabicyclo[3.3.1]nonan-9-yl, 3-oxa-9-azabicyclo[3.3.1]nonan-9-yl and 3-thia-9-azabicyclo[3.3.1]nonan-9-yl.

The group derived from the heterocyclic spiro compound includes e.g. 1,4-dioxa-8-azaspiro[4.5]-decan-8-yl, 1,4-dioxa-7-azaspiro[4.4]decan-7-yl, 1,5-dithia-9-azaspiro[5.5]undecan-9-yl and 1-phenyl-4-oxo-1,3,8-triazaspiro[4.5]decan-8-yl.

It should be understood that the compounds of formula (I) include all of their possible isomers including stereoisomer, metabolite, metabolic precursor and metabolic intermediate.

The compounds of formula (I) can be prepared by various conventional procedures as described below. The compounds of formula (I) are prepared by reacting a compound of formula (II)



(II)

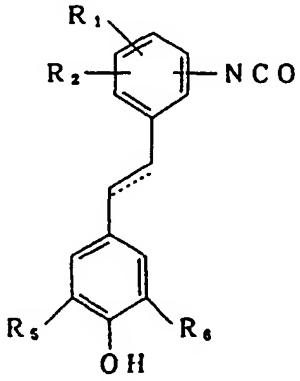
wherein R_1 and R_2 as well as R_5 and R_6 are as defined above, and

denotes -CH_2-CH_2- or -CH=CH- with an isocyanate of formula (III)

R-NCO (III)

wherein R denotes R_3 or R_4, and R_3 and R_4 are as defined above in an organic solvent under ice-cooling or at a temperature up to room temperature. This reaction is performed using the compound of formula (III) in an amount of 0.1 to 10 moles, preferably 0.5 to 2 moles per mole of the compound of formula (II).

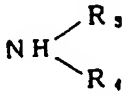
Alternatively, the compounds of formula (I) are prepared by reacting an isocyanate of formula (IV)



(IV)

wherein R_1 and R_2 as well as R_5 and R_6 are as defined above, and

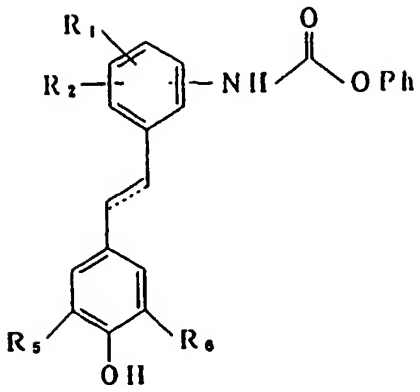
denotes -CH_2-CH_2- or -CH=CH- with an amine of formula (V)



(V)

wherein R denotes R_3 or R_4, and R_3 and R_4 are as defined above in an organic solvent under ice-cooling or at a temperature up to room temperature. This reaction is performed using the compound of formula (V) in an amount of 0.1 to 10 moles, preferably 0.5 to 2 moles per mole of the compound of formula (IV).

Alternatively, the compounds of formula (I) are prepared by reacting a carbamate of formula (VI)

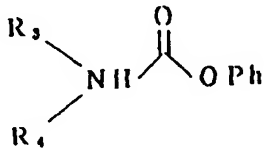


(VI)

wherein R_1 and R_2 as well as R_5 and R_6 are as defined above, and

denotes $-CH_2-CH_2-$ or $-CH=CH-$ with an amine of formula (V) wherein R denotes R_3 or R_4, and R_3 and R_4 are as defined above in an organic solvent while heating at 50-150°C. This reaction is performed using the compound of formula (V) in an amount of 0.1 to 10 moles, preferably 0.5 to 2 moles per mole of the compound of formula (VI).

Alternatively, the compounds of formula (I) are prepared by reacting a compound of formula (II) with a carbamate of formula (VII)



(VII)

wherein R denotes R_3 or R_4, and R_3 and R_4 are as defined above in an organic solvent while heating to 50-150°C. This reaction is performed using the compound of formula (VII) in an amount of 0.1 to 10 moles, preferably 0.5 to 2 moles per mole of the compound of formula (II).

The isocyanates of formula (III) or (IV) are prepared, for example, by treating a carboxylic acid of formula RCOOH wherein R denotes R_3 or R_4, and R_3 and R_4 are as defined above or a derivative thereof with 1 to 10 moles, preferably 1 to 3 moles of diphenylphosphoryl azide, trimethylsilylazide or the like, per mole of the carboxylic acid, in an organic solvent to give an acyl azide, which is in turn subjected to a rearrangement reaction under heating at 50-150°C, or alternatively by reacting a compound of formula (V) or (II) with phosgen.

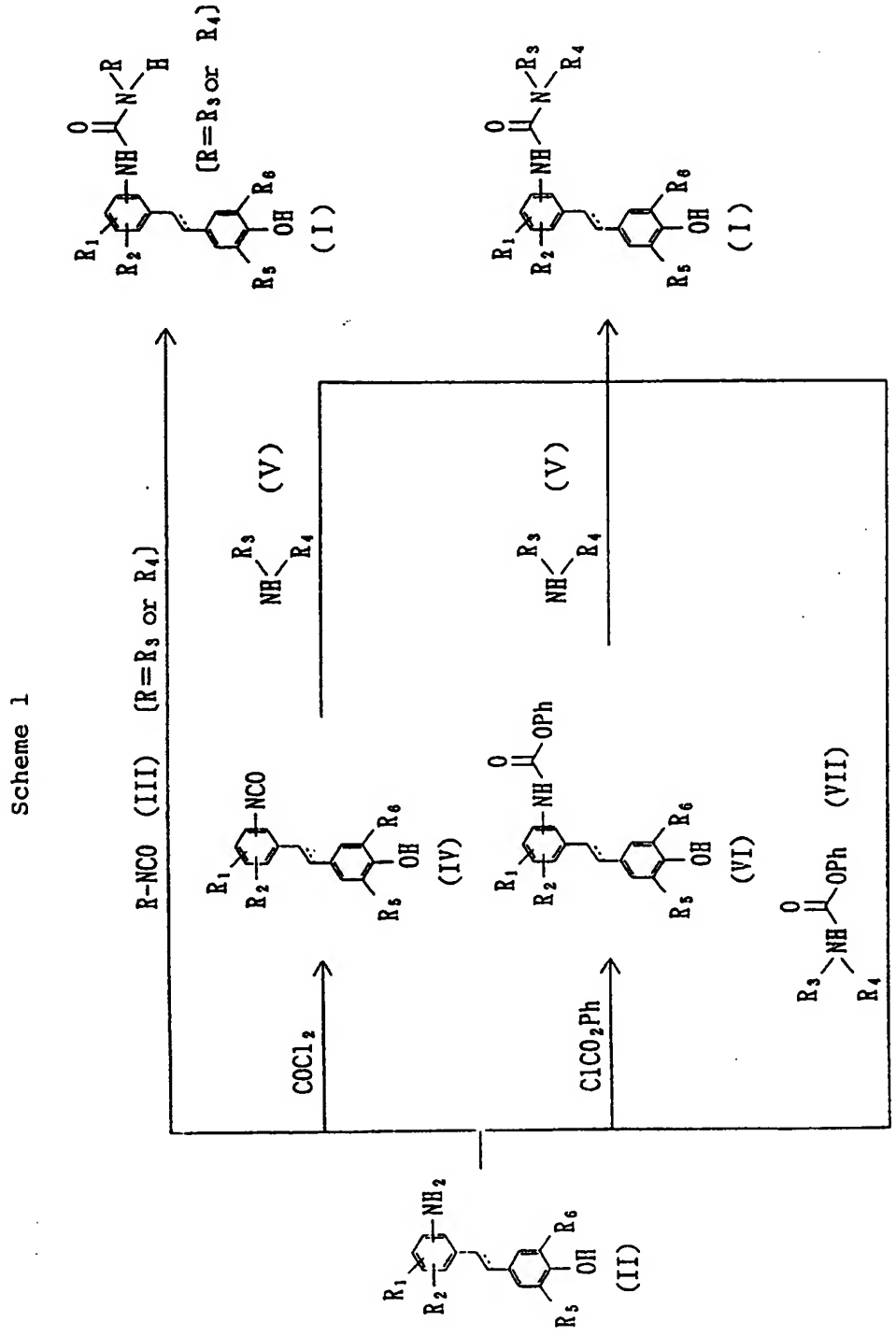
The carbamate of formula (VI) or (VII) are prepared by reacting a compound of formula (II) or (V) with 0.1 to 10 moles, preferably 0.5 to 2 moles of phenyl chloroformate per mole of the compound in an organic solvent under ice-cooling or at a temperature up to room temperature. This reaction may be conducted in the presence of an acid binder. The acid binders include e.g. inorganic basic substances such as sodium hydride, potassium hydroxide, sodium carbonate, potassium carbonate and organic basic substances including secondary amines such as diisopropylamine and tertiary amines such as triethylamine, methylmorpholine, pyridine.

The organic solvents used in each of the above-described reactions include aliphatic hydrocarbon solvents such as hexane, petroleum ether and cyclohexane, aromatic hydrocarbon solvents such as benzene, toluene and xylenes, halogenated hydrocarbon solvents such as methylene chloride, chloroform, carbon tetrachloride and dichloroethane, ether solvents such as ethyl ether, isopropyl ether, tetrahydrofuran and dioxane, ketone solvents such as acetone and

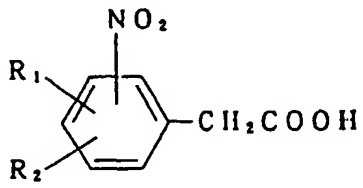
methyl ethyl ketone, ethyl acetate, acetonitrile and N,N-dimethylformamide.

The process steps for the compounds of the invention according to the reactions as described above are shown in the following scheme 1:

Scheme 1

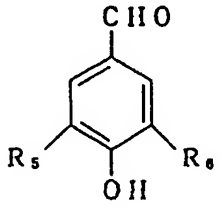


The compounds of formula (II) are prepared by reacting a nitrophenylacetic acid derivative of formula (IX)



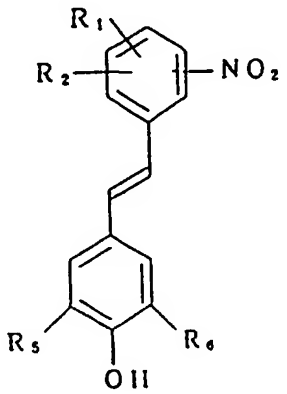
(IX)

wherein R_1 and R_2 are as defined above with a benzaldehyde derivative of formula (VIII)



(VIII)

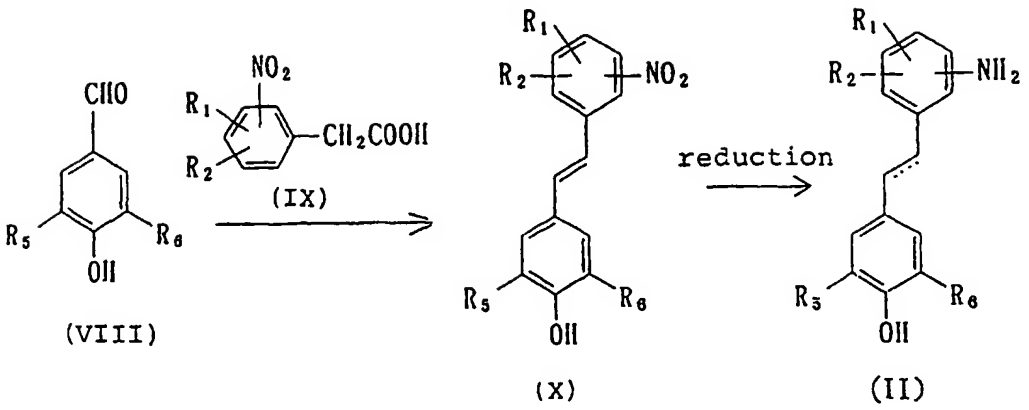
wherein R_5 and R_6 are as defined above while heating at 100 to 200°C in the presence of a catalytic amount of a basic material such as piperidine, to form a compound of formula (X)



(X)

wherein R_5 and R_6 are as defined above, followed by reduction. The reaction is performed using the compound of formula (VIII) in an amount of 0.1 to 10 moles, preferably. 0.5 to 2 moles per mole of the compound of formula (IX). The reduction process includes e.g. that using zinc, iron, tin, stannous chloride or the like in an acidic solution such as hydrochloric acid, acetic acid or a catalytic hydrogenation using a catalyst such as palladium carbon, platinum oxide or the like. The process steps by the reactions as described above are shown in the following scheme 2:

Scheme 2



Pharmaceutically acceptable salts of the compounds of formula (I) may be formed in conventional way. The acid addition salts may be formed for example by reaction of the base compound of formula (I) with a pharmaceutically acceptable inorganic acid such as hydrochloric, hydrobromic, hydroiodic, sulfuric and phosphoric acids or a pharmaceutically acceptable organic acid such as oxalic, maleic, fumaric, lactic, malic, citric, tartaric, benzoic and methanesulphonic acids.

The compounds of formula (I) according to the present invention possess both an ACAT inhibitor activity and an antioxidative activity, especially a protective ability against an oxidative modification of LDL. By the ACAT inhibitory activity, the present compounds can inhibit an absorption of cholesterol from the intestinal tracts, reduce a plasma cholesterol level and inhibit an accumulation of cholesteryl esters in the wall of blood vessels, atheroma lesion and macrophage. By the antioxidative activity, especially a protective activity against the oxidative modification of LDL, the present compounds can inhibit the formation and progression of atherosclerosis lesion and inducing its regression.

Thus, the compounds of the present invention are useful in the prophylaxis or treatment of hypercholesterolemia and atherosclerosis.

According to another aspect of the present invention, there is provided an ACAT inhibitor comprising the compound of formula (I) or a pharmaceutically acceptable salt thereof.

In further aspects, the present invention provides a pharmaceutical composition for the prophylaxis or treatment of hypercholesterolemia or atherosclerosis, which comprises as an active ingredient the compound of formula (I) or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier and/or excipient.

The compounds of the invention can usually be administered orally or parenterally in the form of a pharmaceutical preparation. The pharmaceutical preparations include tablets, capsules, troches, syrups, granules, powders, injections, suspensions and the like. It may be in bilayered or multilayered tablet with other drugs. The tablets may also be coated with a conventional coating to form, e.g., sugar-coated, enteric-coated or film-coated tablets.

In preparing solid preparations, additives such as lactose, refined sugar, crystalline cellulose, corn starch, calcium phosphate, sorbitol, glycin, carboxymethylcellulose, gum arabic, polyvinylpyrrolidone, hydroxypropylcellulose, polyethylene glycol, stearic acid, magnesium stearate and talc are employed.

A vegetable or synthetic wax or fat or a similar base is used in preparing the semi-solid preparations.

As additives in preparing the liquid preparations are used, for example, sodium chloride, sorbitol, glycerin, olive oil, almond oil, propylene glycol and ethyl alcohol.

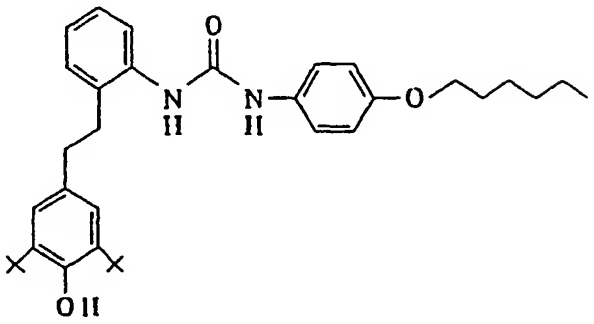
The active ingredient is contained in the formulation in an amount of 0.0001-100% by weight, suitably 0.001-50% by weight in the case of formulations for oral administration and 0.0001-10% by weight in the case of formulations for injection based on the weight of the preparations.

Route and dosage of administration for the compounds of the invention are not specifically limited and are appropriately chosen depending upon form of the formulation, age and sex of the patient, severity of the disease and other factors. Daily dosage of the active ingredient is 0.01-1000 mg. No adverse toxicological effects are indicated at any of the above dosage ranges.

The invention is further illustrated by the following examples.

Example 1

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-hexyloxyphenyl)urea

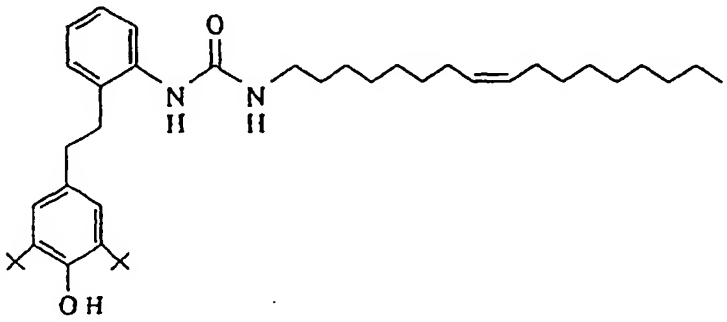


A solution of diphenylphosphorylazide (0.93 g, 3.4 mmol), 4-hexyloxybenzoic acid (0.68 g, 3.1 mmol) and triethylamine (0.34 g, 3.4 mmol) in toluene (10 ml) was stirred at room temperature for 3.5 hrs and heated at about 90°C for 2 hrs with stirring. After allowing the mixture to cool (under 0°C), a solution of 4-(2-aminophenethyl)-2,6-di-tert-butylphenol (1.0 g, 3.1 mmol) in toluene (4 ml) was added dropwise. The solution was warmed up to room temperature and stirred overnight. After distilling off the solvent and purification of the residue by a silica gel column chromatography, recrystallization from ethyl acetate/hexane afforded N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-hexyloxyphenyl)urea (1.2 g, 71% yield). m.p. 174-176°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.40-7.42(m, 1H), 7.14-7.26(m, 5H), 6.81(s, 2H), 6.76-6.79(m, 2H), 5.98(s, 1H), 5.39(s, 1H), 5.13(s, 1H), 3.88(t, J=7Hz, 2H), 2.83-2.87(m, 2H), 2.76-2.80(m, 2H), 1.70-1.77(m, 2H), 1.38(s, 18H), 1.30-1.45(m, 6H), 0.87-0.93(m, 3H)
IR (cm^{-1}) 3640, 3310, 2950, 1630, 1560, 1490, 1440, 1230

Example 2

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(8-heptadecenyl)urea



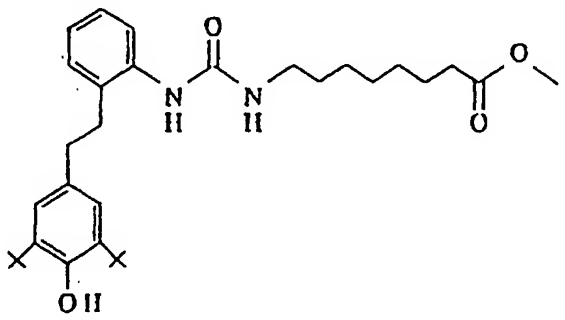
The title compound was prepared in a similar manner to that mentioned in Example 1, using 9-octadecenoic acid instead of 4-hexyloxybenzoic acid.

^{1}H-NMR (δ ppm, $CDCl_3$) 7.16-7.26(m, 4H), 6.78(s, 2H), 5.29-5.34(m, 2H), 5.12(s, 1H), 5.00(s, 1H), 4.19(t, J=6Hz,

1H), 3.11(dd, J=14, 6Hz, 2H), 2.77-2.87(m, 4H), 1.93-2.02(m, 4H), 1.38(s, 18H), 1.18-1.38(m, 25H)
IR (cm^{-1}) 3642, 3288, 2926, 1639, 1558, 1435, 1233, 750

Example 3

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(7-methoxycarbonylheptyl)urea

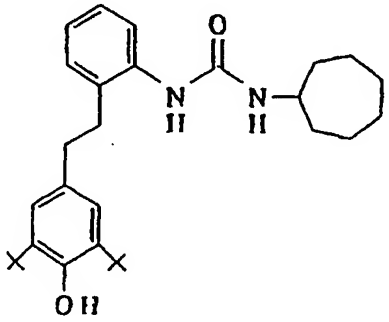


The title compound was prepared in a similar manner to that mentioned in Example 1, using 8-methoxycarbonyloctanoic acid instead of 4-hexyloxybenzoic acid

^{1}H-NMR (δ ppm, $CDCl_3$) 7.16-7.26(m, 4H), 6.78(s, 2H), 5.12(s, 1H), 4.98(s, 1H), 4.17(t, J=6Hz, 1H), 3.66(s, 3H), 3.09-3.14(m, 2H), 2.77-2.87(m, 4H), 2.28(t, J=8Hz, 2H), 1.53-1.61(m, 2H), 1.38(s, 18H), 1.18-1.30(m, 6H), 0.88(t, J=7Hz, 2H)
IR (cm^{-1}) 3640, 2928, 1737, 1639, 1547, 1436, 1234

Example 4

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-cycloheptylurea

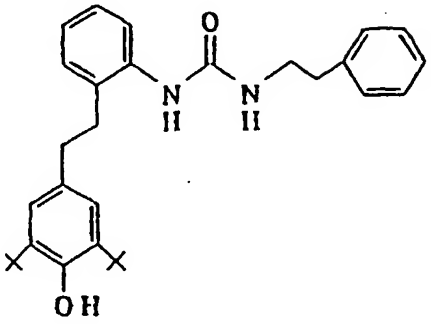


The title compound was prepared in a similar manner to that mentioned in Example 1, using cycloheptanecarboxylic acid instead of 4-hexyloxybenzoic acid. m.p. 177-178°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.17-7.26(m, 4H), 6.79(s, 2H), 5.10(s, 1H), 5.05(bs, 1H), 4.19(d, J=8Hz, 1H), 3.75-3.85(m, 1H), 2.80-2.88(m, 2H), 2.75-2.80(m, 2H), 1.83-1.90(m, 2H), 1.38(s, 18H), 1.21-1.58(m, 10H)
IR (cm^{-1}) 3650, 3300, 2930, 2860, 1630, 1570, 1440, 1240

Example 5

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-phenethylurea

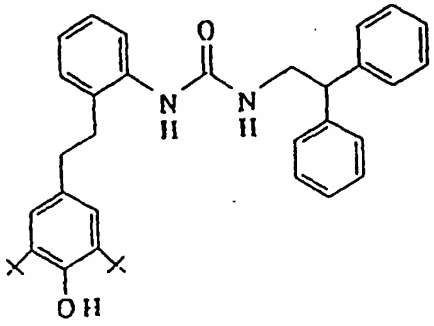


The title compound was prepared in a similar manner to that mentioned in Example 1, using 3-phenylpropionic acid instead of 4-hexyloxybenzoic acid.
m.p. 197-198°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.08-7.25(m, 9H), 6.76(s, 2H), 5.10(s, 1H), 5.00(s, 1H), 4.24(t, J=6Hz, 1H), 3.36-3.41(m, 2H), 2.72-2.80(m, 6H), 1.36(s, 18H)
IR (cm^{-1}) 3632, 3284, 2954, 1640, 1559, 1436, 1235, 748

Example 6

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(2,2-diphenylethyl)urea

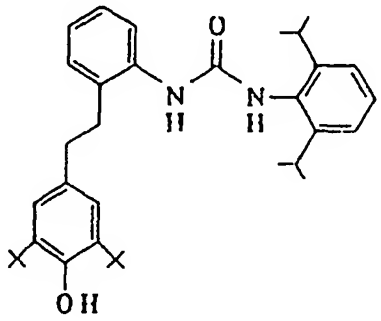


The title compound was prepared in a similar manner to that mentioned in Example 1, using 3,3-diphenylpropionic acid instead of 4-hexyloxybenzoic acid.
m.p. 179°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.09-7.44(m, 12H), 6.97-7.01(m, 1H), 6.78(d, J=8Hz, 1H), 6.72(s, 2H), 5.07(s, 1H), 4.93(s, 1H), 4.23(t, J=6Hz, 1H), 4.15(t, J=8Hz, 1H), 3.77(dd, J=8, 6Hz, 2H), 2.70(s, 4H), 1.35(s, 18H)
IR (cm^{-1}) 3644, 2930, 1650, 1553, 1510, 1234

Example 7

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(2,6-diisopropylphenyl)urea

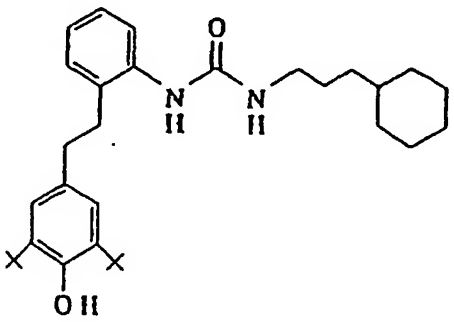


The title compound was prepared in a similar manner to that mentioned in Example 1, using 2,6-diisopropylbenzoic acid instead of 4-hexyloxybenzoic acid.
m.p. 209-210°C

^{1}H-NMR (δ ppm, DMSO) 8.01(bs, 1H), 7.85(bs, 1H), 7.65(d, J=8Hz, 1H), 7.20-7.24(m, 1H), 7.10-7.14(m, 4H), 6.93-6.97(m, 3H), 6.62(s, 1H), 3.32-3.53(m, 1H), 3.18-3.25(m, 1H), 2.75-2.85(m, 4H), 1.37(s, 18H), 1.13(d, J=7Hz, 12H)
IR (cm^{-1}) 3612, 3320, 2958, 1646, 1586, 1534, 1435, 1231, 745

Example 8

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(3-cyclohexylpropyl)urea

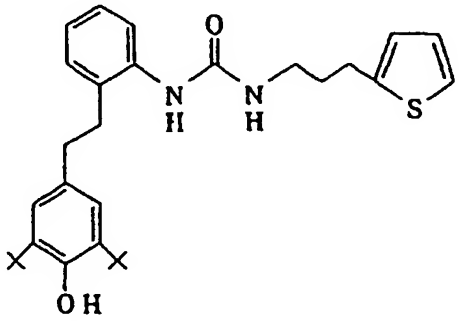


The title compound was prepared in a similar manner to that mentioned in Example 1, using 4-cyclohexylbutanoic acid instead of 4-hexyloxybenzoic acid.
m.p. 166°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.18-7.26(m, 4H), 6.78(s, 2H), 5.11(s, 1H), 5.02(s, 1H), 4.20(t, 1H), 3.10 (dt, J=6, 7Hz, 2H), 2.83-2.85(m, 2H), 2.76-2.80(m, 2H), 1.56-1.68(m, 4H), 1.38(s, 18H), 1.33-1.43(m, 2H), 1.04-1.30(m, 6H), 0.75-0.88(m, 3H)
IR (cm^{-1}) 3640, 3316, 2924, 1640, 1558, 1436, 1233, 749

Example 9

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[3-(2-thienyl)propyl]urea

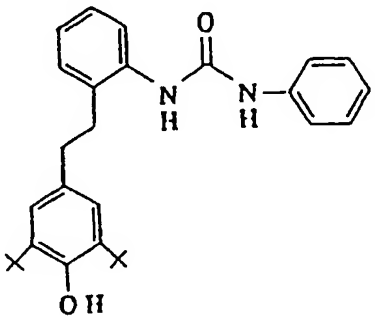


The title compound was prepared in a similar manner to that mentioned in Example 1, using 4-(2-thienyl)butanoic acid instead of 4-hexyloxybenzoic acid.
m.p. 150°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.19-7.27(m, 4H), 7.07(dd, J=4, 1Hz, 1H), 6.87(dd, J=3, 2Hz, 1H), 6.77(s, 2H), 6.71(t, J=2Hz, 1H), 5.11(s, 1H), 4.96(s, 1H), 4.21(t, 1H), 3.20(s, 2H), 2.77-2.87(m, 6H), 1.81(qui, J=7Hz, 2H), 1.37(s, 18H)
IR (cm^{-1}) 3638, 3286, 2918, 1630, 1570, 1434, 1233, 696

Example 10

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-phenylurea

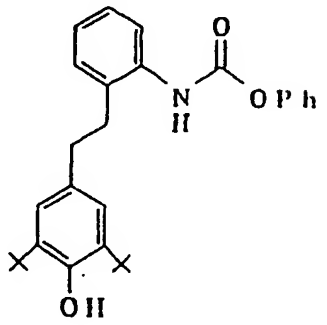


The title compound was prepared in a similar manner to that mentioned in Example 1, using benzoic acid instead of 4-hexyloxybenzoic acid. m.p. 207°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.22-7.36(m, 8H), 7.02(t, J=7Hz, 1H), 6.80(s, 2H), 6.02(s, 1H), 5.18(s, 1H), 5.15(s, 1H), 2.79-2.91(m, 4H), 1.38(s, 18H)
IR (cm^{-1}) 3630, 3350, 2950, 1650, 1600, 1550, 1500, 1230, 750

Example 11

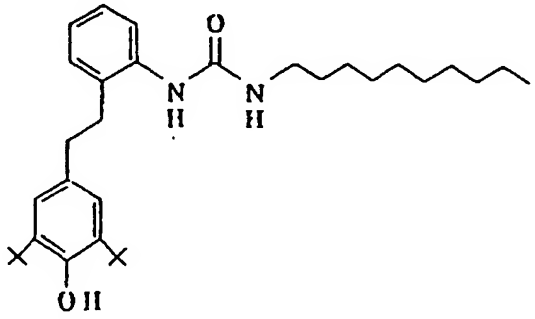
(1) N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]phenyl carbamate



To a solution of 4-(2-aminophenethyl)-2,6-di-tert-butylphenol (7.00 g, 21.5 mmol) and diisopropylamine (3.4 ml, 24 mmol) in dichloromethane (50 ml) was added dropwise a solution of phenyl chloroformate (3.60 g, 23.0 mmol) in dichloromethane (10 ml) so that the internal temperature does not exceed 0°C over a ice-cold water bath. The mixture was stirred at the same temperature for 2 hrs, washed with water, dried over $MgSO_4$ and concentrated. Purification of the residue by a silica gel column chromatography gave a viscous oil of N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]phenyl carbamate (8.16 g, 85.2% yield).

^{1}H-NMR (δ ppm, $CDCl_3$) 7.63(bs, 1H), 7.34(t, J=8Hz, 2H), 7.08-7.29(m, 6H), 6.80(s, 2H), 5.74(bs, 1H), 5.13(s, 1H), 2.8-2.9(m, 4H), 1.35(s, 18H)

(2) N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-decylurea

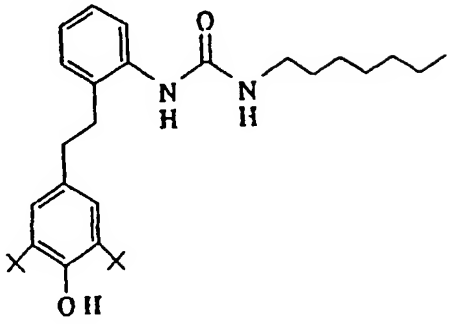


A solution of N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]phenyl carbamate (1.0 g, 2.2 mmol) and decylamine (0.38 g, 2.4 mmol) in xylene (10 ml) was heated under reflux for 2.5 hrs. After distilling off the solvent, purification of the residue by a silica gel column chromatography afforded waxy N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-decylurea (0.93 g, 85% yield).

^{1}H-NMR (δ ppm, $CDCl_3$) 7.17-7.26(m, 4H), 6.78(s, 2H), 5.11(s, 1H), 4.98(s, 1H), 4.17(t, J=6Hz, 1H), 3.09-3.16(m, 2H), 2.76-2.87(m, 4H), 1.50-2.50(m, 16H), 1.38(s, 18H), 0.87(t, J=7Hz, 3H)
IR (cm^{-1}) 3650, 3350, 2960, 2930, 2850, 1640, 1570

Example 12

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-heptylurea

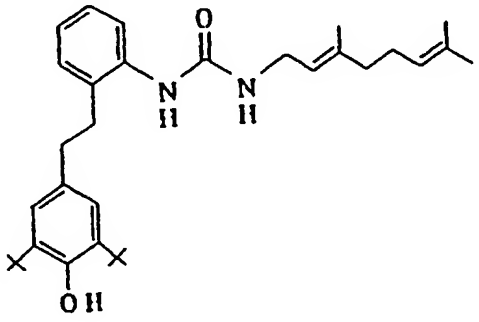


The title compound was prepared in a similar manner to that mentioned in Example 11, using heptylamine instead of decylamine. m.p. 100°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.18-7.27(m, 4H), 6.78(s, 2H), 5.11(s, 1H), 4.99(s, 1H), 4.18(bt, J=5Hz, 1H), 2.89(q, J=6Hz, 2H), 2.79-2.85(m, 4H), 1.38-1.45(m, 2H), 1.38(s, 18H), 1.15-1.30(m, 8H), 0.86(t, J=7Hz, 3H)
IR (cm^{-1}) 3650, 3320, 2970, 2940, 2870, 1640, 1570, 1440, 1240, 760

Example 13

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(3,7-dimethyl-2,6-octadienyl)urea

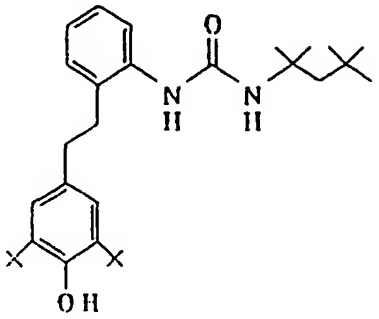


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3,7-dimethyl-2,6-octadienylamine instead of decylamine. m.p. 87.0-87.5°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.16-7.30(m, 4H), 6.78(s, 2H), 5.10(s, 1H), 5.05-5.13(m, 1H), 5.02(bs, 2H), 4.05-4.12(m, 1H), 3.75(t, J=6Hz, 2H), 2.80-2.85(m, 2H), 2.75-2.80(m, 2H), 1.95-2.08(m, 2H), 1.89-1.95(m, 2H), 1.65(s, 3H), 1.60(s, 3H), 1.57(s, 3H), 1.37(s, 18H)
IR (cm^{-1}) 3628, 3312, 2956, 1638, 1585, 1436, 1233, 752

Example 14

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(2,4,4-trimethyl-2-pentyl)urea

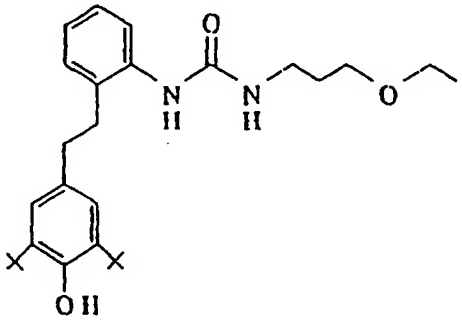


The title compound was prepared in a similar manner to that mentioned in Example 11, using 2,2,4-trimethyl-2-pentylamine instead of decylamine. m.p. 168-169°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.15-7.26(m, 4H), 6.83(s, 2H), 5.09(s, 2H), 4.18(s, 1H), 2.71-2.87(m, 4H), 1.64(s, 2H), 1.39(s, 18H), 1.34(s, 6H), 0.90(s, 9H)
IR (cm^{-1}) 3640, 3334, 2956, 1645, 1556, 1437, 1365, 1226

Example 15

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(3-ethoxypropyl)urea

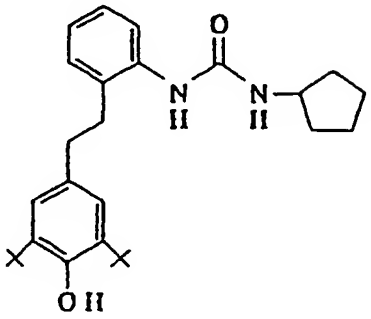


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3-ethoxypropylamine instead of decylamine. m.p. 136-137°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.16-7.27(m, 4H), 6.79(s, 2H), 5.10(s, 1H), 5.06(s, 1H), 4.78(t, J=5Hz, 1H), 3.40(t, J=6Hz, 2H), 3.32(dd, J=14, 7Hz, 2H), 3.28(q, J=6Hz, 2H), 2.84-2.88(m, 2H), 2.77-2.80(m, 2H), 1.67-1.73(m, 2H), 1.38(s, 18H), 0.99(t, J=7Hz, 3H)
IR (cm^{-1}) 3600, 3346, 2952, 1638, 1563, 1436, 1288, 1238, 1108, 753

Example 16

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-cyclopentylurea

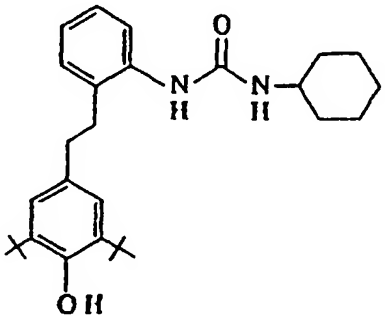


The title compound was prepared in a similar manner to that mentioned in Example 11, using cyclopentylamine instead of decylamine. m.p. 186-187°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.15-7.28(m, 4H), 6.79(s, 2H), 5.11(s, 1H), 5.08(s, 1H), 4.17(d, J=7Hz, 1H), 4.01-4.10(m, 1H), 2.76-2.87(m, 4H), 1.89-1.96(m, 2H), 1.50-1.61(m, 4H), 1.39(s, 18H), 1.22-1.29(m, 2H)
IR (cm^{-1}) 3650, 3350, 2950, 1640, 1580, 1560, 1440, 1240

Example 17

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-cyclohexylurea

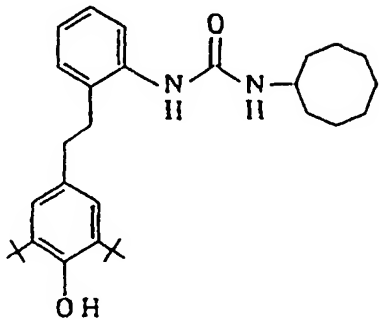


The title compound was prepared in a similar manner to that mentioned in Example 11, using cyclohexylamine instead of decylamine. m.p. 198-200°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.16-7.25(m, 4H), 6.78(s, 2H), 5.14(s, 1H), 4.99(s, 1H), 4.09(d, J=5Hz, 1H), 3.59-3.62(m, 1H), 2.83(d, J=6Hz, 2H), 2.79(d, J=6Hz, 2H), 1.95-1.99(m, 2H), 1.53-1.64(m, 4H), 1.38(s, 18H), 1.26-1.30(m, 2H), 0.96-0.99(m, 2H)
IR (cm^{-1}) 3290, 2930, 1630, 1561, 1232

Example 18

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-cyclooctylurea

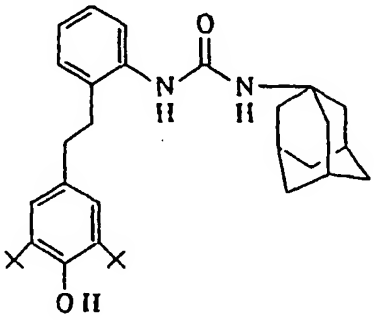


The title compound was prepared in a similar manner to that mentioned in Example 11, using cyclooctylamine instead of decylamine. m.p. 174-176°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.17-7.24(m, 4H), 6.79(s, 2H), 5.10(s, 1H), 5.05(s, 1H), 4.19(d, J=5Hz, 1H), 3.68-3.98(m, 1H), 2.83(d, J=6Hz, 2H), 2.79(d, J=6Hz, 2H), 1.74-1.81(m, 2H), 1.42-1.58(m, 12H), 1.38(s, 18H)
IR (cm^{-1}) 3308, 2922, 1630, 1554, 1435, 1233

Example 19

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-adamantylurea

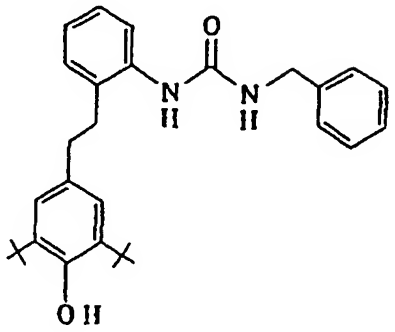


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-adamantanamine instead of decylamine. m.p. 197-199°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.14-7.29(m, 4H), 6.83(s, 2H), 5.11(s, 1H), 5.10(s, 1H), 4.06(s, 1H), 2.79-2.85(m, 4H), 1.91-2.05(m, 9H), 1.60-1.70(m, 6H), 1.39(s, 18H)
IR (cm^{-1}) 3350, 2900, 2850, 1640, 1550, 1440, 1300, 1240

Example 20

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-benzylurea

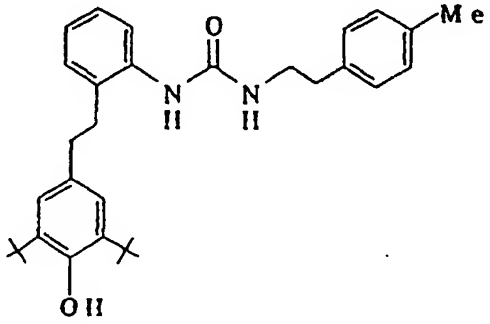


The title compound was prepared in a similar manner to that mentioned in Example 11, using benzylamine instead of decylamine. m.p. 181-183°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.15-7.30(m, 9H), 6.77(s, 2H), 5.13(s, 1H), 5.08(s, 1H), 4.54(t, J=6Hz, 1H), 4.33(d, J=6Hz, 2H), 2.82(d, J=6Hz, 2H), 2.78(d, J=6Hz, 2H), 1.35(s, 18H)
IR (cm^{-1}) 3294, 2956, 1629, 1579, 1435, 1233, 741

Example 21

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-methylphenethyl)urea

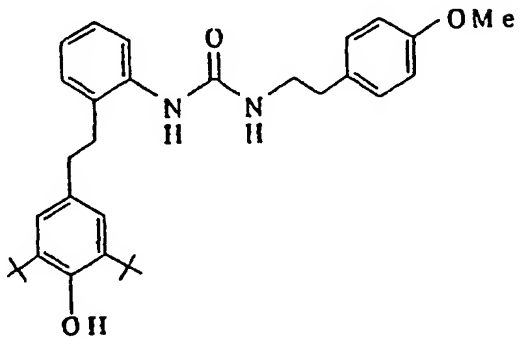


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-methylphenethylamine instead of decylamine.
m.p. 170-172°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.12-7.23(m, 4H), 7.04(d, J=8Hz, 2H), 6.98(d, J=8Hz, 2H), 6.76(s, 2H), 5.09(s, 1H), 4.96(s, 1H), 4.22(t, J=6Hz, 1H), 3.36(q, J=6Hz, 2H), 2.80(d, J=6Hz, 2H), 2.69(t, J=6Hz, 2H), 2.68(d, J=6Hz, 2H), 2.29(s, 3H), 1.36(s, 18H)
IR (cm^{-1}) 3342, 2950, 1643, 1563, 1435

Example 22

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-methoxyphenethyl)urea

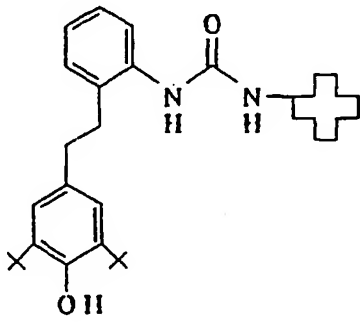


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-methoxyphenethylamine instead of decylamine.
m.p. 148-149°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.10-7.24(m, 4H), 7.00(d, J=9Hz, 2H), 6.77(d, J=9Hz, 2H), 6.76(s, 2H), 5.09(s, 1H), 4.95(s, 1H), 4.20(t, J=6Hz, 1H), 3.76(s, 3H), 3.33(q, J=6Hz, 2H), 2.80(d, J=6Hz, 2H), 2.77(d, J=6Hz, 2H), 2.67(t, J=6Hz, 2H), 1.36(s, 18H)
IR (cm^{-1}) 3420, 2960, 1641, 1561, 1525, 1249

Example 23

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-cyclododecylurea

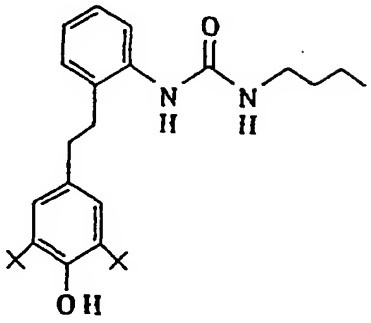


The title compound was prepared in a similar manner to that mentioned in Example 11, using cyclododecylamine instead of decylamine.

^{1}H-NMR (δ ppm, $CDCl_3$) 7.06-7.29(m, 4H), 6.80(s, 2H), 5.10(s, 2H), 4.05(d, J=9Hz, 1H), 3.89(s, 1H), 2.76-2.87(m, 4H), 1.38(s, 18H), 1.20-1.30(m, 22H)
IR (cm^{-1}) 3650, 3340, 2950, 2920, 1640, 1560, 1440, 1240

Example 24

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-butylurea

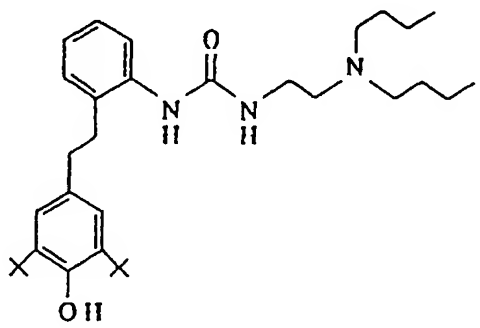


The title compound was prepared in a similar manner to that mentioned in Example 11, using butylamine instead of decylamine. m.p. 133-134°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.16-7.26(m, 4H), 6.78(s, 2H), 5.12(s, 1H), 4.97(s, 1H), 4.16(t, J=6Hz, 1H), 3.11-3.16(m, 2H), 2.77-2.87(m, 4H), 1.38(s, 18H), 1.21-1.34(m, 4H), 0.87(t, J=7Hz, 3H)
IR (cm^{-1}) 3450, 3320, 2960, 1640, 1570, 1460, 1440, 1250, 1230

Example 25

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[2-(N,N-dibutylamino)ethyl]urea



The title compound was prepared in a similar manner to that mentioned in Example 11, using N,N-dibutylethylenediamine instead of decylamine.

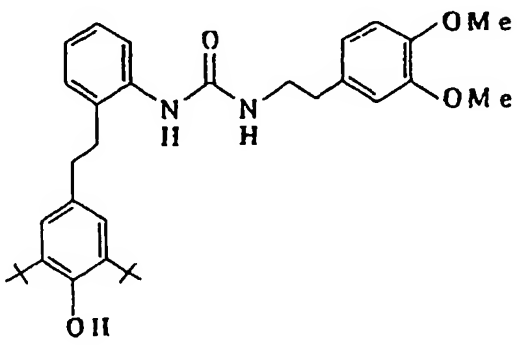
^{1}H-NMR (δ ppm, $CDCl_3$) 7.18-7.26(m, 4H), 6.80(s, 2H), 5.18(s, 1H), 5.10(s, 1H), 5.02(bs, 1H), 3.17-3.21(m, 2H), 2.76-2.87(m, 4H), 2.40(t, J=6Hz, 2H), 2.24(t, J=7Hz, 4H), 1.38(s, 18H), 1.04-1.26(m, 8H), 0.82(t, J=7Hz, 6H)
IR (cm^{-1}) 3650, 3360, 2960, 2880, 1640, 1560, 1440, 1240

Further, the hydrochloride of the title compound was prepared in the following manner.

Conc. hydrochloric acid (0.17 ml) was added to a solution of the title compound (0.95 g) in ethanol (12 ml). Distilling off the solvent afforded a waxy hydrochloride of the title compound (1.05 g).

Example 26

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(3,4-dimethoxyphenethyl)urea

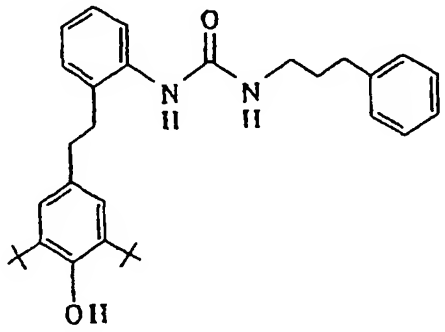


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3,4-dimethoxyphenethylamine instead of decylamine. m.p. 158-160°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.10-7.24(m, 4H), 6.76(s, 2H), 6.70-6.75(m, 1H), 6.60-6.65(m, 2H), 5.10(s, 1H), 5.00(s, 1H), 4.27(t, J=6Hz, 1H), 3.83(s, 3H), 3.81(s, 3H), 3.35-3.40(dt, J=6, 7Hz, 2H), 2.72-2.84(m, 4H), 2.68(t, J=7Hz, 2H), 1.36(s, 18H)
IR (cm^{-1}) 3628, 3318, 1632, 1562, 1518, 1264, 1234

Example 27

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(3-phenylpropyl)urea

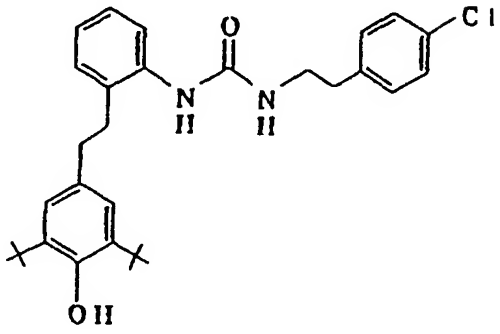


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3-phenylpropylamine instead of decylamine. m.p. 161-162°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.13-7.25(m, 7H), 7.10(d, J=8Hz, 2H), 6.77(s, 2H), 5.10(s, 1H), 4.98(s, 1H), 4.20(t, J=7Hz, 1H), 3.17(q, J=7Hz, 2H), 2.83(d, J=6Hz, 2H), 2.79(d, J=6Hz, 2H), 2.56(t, J=7Hz, 2H), 1.74(qui, J=7Hz, 2H), 1.36(s, 18H)
IR (cm^{-1}) 3628, 3328, 2952, 1637, 1562, 1435, 1234, 748, 697

Example 28

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-chlorophenethyl)urea

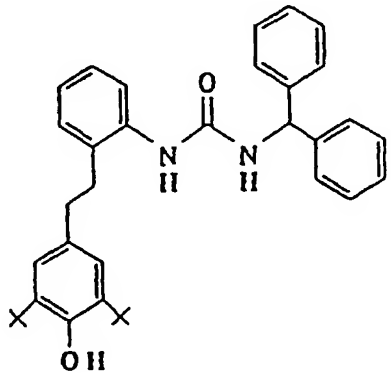


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-chlorophenethylamine instead of decylamine. m.p. 173-174°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.09-7.20(m, 6H), 7.02(d, 2H), 6.75(s, 2H), 5.10(s, 1H), 4.91(s, 1H), 4.16(t, J=6Hz, 1H), 3.35(q, J=6Hz, 2H), 2.78(q, J=5Hz, 4H), 2.70(t, J=7Hz, 2H), 1.35(s, 18H)
IR (cm^{-1}) 3626, 3322, 2950, 1638, 1561, 1493, 1436, 1234

Example 29

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-diphenylmethylurea

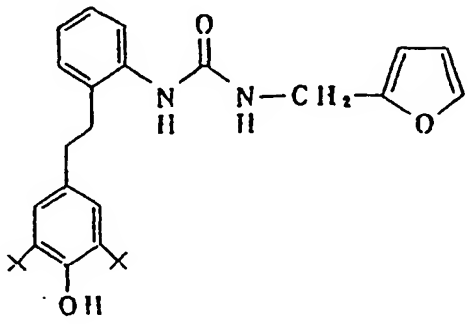


The title compound was prepared in a similar manner to that mentioned in Example 11, using benzhydrylamine instead of decylamine. m.p. 187.4°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.14-7.33(m, 14H), 6.75(s, 2H), 6.10(d, J=8Hz, 1H), 5.17(s, 1H), 5.08(s, 1H), 4.86(d, J=8Hz, 1H), 2.73-2.81(m, 4H), 1.35(s, 18H)
IR (cm^{-1}) 2960, 1640, 1560, 1500, 1460, 1440, 1240, 740, 700

Example 30

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[(2-furyl)methyl]urea

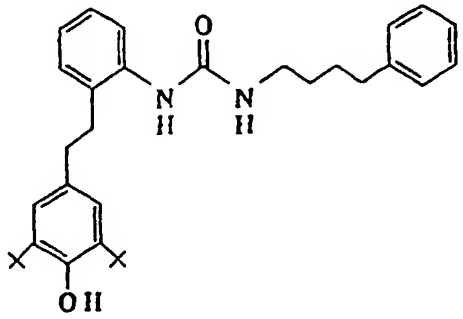


The title compound was prepared in a similar manner to that mentioned in Example 11, using 2-aminomethylfuran instead of decylamine. m.p. 169.7°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.15-7.28(m, 5H), 6.76(s, 2H), 6.26-6.27(m, 1H), 6.14-6.15(m, 1H), 5.10(s, 1H), 4.99(s, 1H), 4.45(t, J=6Hz, 1H), 4.32(d, J=6Hz, 2H), 2.76-2.86(m, 4H), 1.36(s, 18H)
IR (cm^{-1}) 3320, 2950, 1640, 1590, 1570, 1460, 1440, 1240, 730

Example 31

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-phenylbutyl)urea

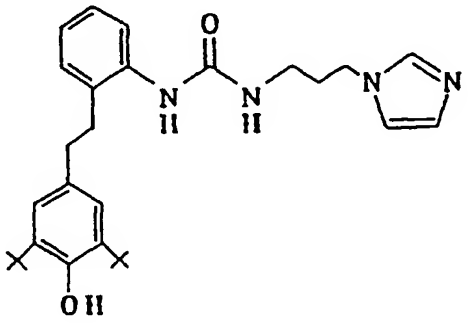


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-phenylbutylamine instead of decylamine. m.p. 157.0°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.11-7.27(m, 9H), 6.77(s, 2H), 5.10(s, 1H), 4.95(s, 1H), 4.15(t, 1H), 3.12-3.17(m, 2H), 2.74-2.86(m, 4H), 2.58(t, J=8Hz, 2H), 1.39-1.61(m, 4H), 1.37(s, 18H)
IR (cm^{-1}) 3300, 2950, 2860, 1620, 1600, 1580, 1440, 1250, 1240

Example 32

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[3-(1-imidazolyl)propyl]urea

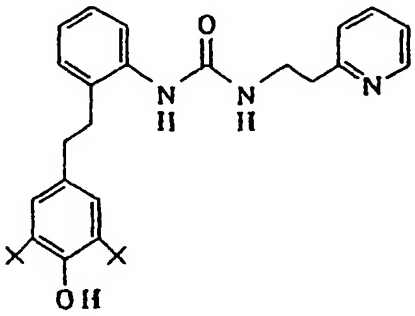


The title compound was prepared in a similar manner to that mentioned in Example 11, using N-(3-aminopropyl)imidazole instead of decylamine.
m.p. 163.5°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.39(s, 1H), 7.20-7.29(m, 4H), 7.01(s, 1H), 6.85-6.86(m, 1H), 6.77(s, 2H), 5.15(s, 1H), 4.97(s, 1H), 4.25(t, J=6Hz, 1H), 3.92(t, J=7Hz, 2H), 3.13(dt, J=8, 7Hz, 2H), 2.77-2.86(m, 4H), 1.88-1.95(m, 2H), 1.37(s, 18H)
IR (cm^{-1}) 3360, 3320, 2960, 1640, 1570, 1520, 1440, 1240

Example 33

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[2-(2-pyridyl)ethyl]urea

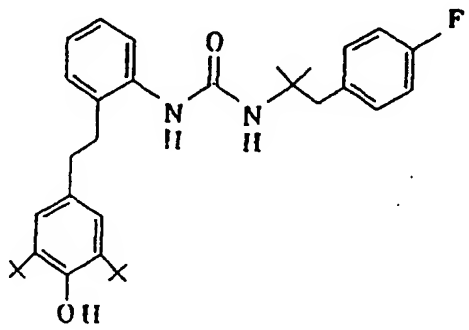


The title compound was prepared in a similar manner to that mentioned in Example 11, using 2-(2-aminoethyl)pyridine instead of decylamine.
m.p. 179.7°C

^{1}H-NMR (δ ppm, $CDCl_3$) 8.32(d, J=4Hz, 1H), 7.52-7.56(m, 1H), 7.06-7.27(m, 6H), 6.77(s, 2H), 5.21(t, J=6Hz, 1H), 5.11(s, 1H), 5.10(s, 1H), 3.56(q, J=6Hz, 2H), 2.93(t, J=6Hz, 2H), 2.67-2.83(m, 4H), 1.37(s, 18H)
IR (cm^{-1}) 3350, 2960, 1650, 1590, 1570, 1440, 760

Example 34

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(4-fluorophenyl)-2-methyl-2-propyl]urea

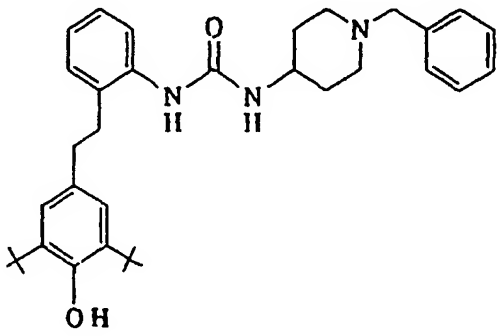


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-fluoro-α,α dimethylphenethylamine instead of decylamine.
m.p. 150.6°C

^{1}H-NMR (δ ppm, $CDCl_3$) 6.84-7.26(m, 8H), 6.80(s, 2H), 5.10(s, 1H), 5.09(s, 1H), 3.95(s, 1H), 2.95(s, 2H), 2.72-2.82(m, 4H), 1.37(s, 18H), 1.25(s, 6H)
IR (cm^{-1}) 3350, 2960, 1640, 1560, 1510, 1440, 1240

Example 35

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-benzyl-4-piperidyl)urea

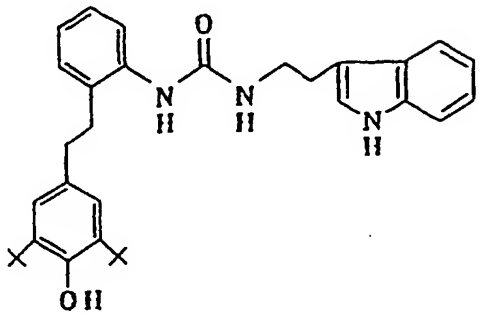


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-benzylpiperidine instead of decylamine. m.p. 79-81°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.20-7.34(m, 9H), 6.77(s, 2H), 5.10(s, 1H), 4.99(s, 1H), 4.07-4.15(m, 1H), 3.58-3.72(m, 1H), 3.44(s, 2H), 2.68-2.86(m, 6H), 2.00-2.10(m, 2H), 1.80-1.90(m, 2H), 1.37(s, 18H), 1.24-1.35(m, 2H)
IR (cm^{-1}) 3632, 3350, 1640, 1552

Example 36

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[2-(3-indolyl)ethyl]urea

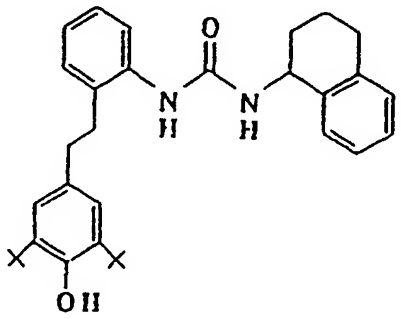


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3-(2-aminoethyl)indole instead of decylamine.
m.p. 193-194°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.92(s, 1H), 7.54(d, J=8Hz, 1H), 7.33(d, J=8Hz, 1H), 7.05-7.26(m, 6H), 6.90(d, J=2Hz, 1H), 6.77(s, 2H), 5.10(s, 1H), 5.00(s, 1H), 4.32(t, J=6Hz, 1H), 3.47(dt, J=6, 7Hz, 2H), 2.90(t, J=7Hz, 2H), 2.73-2.81(m, 4H), 1.35(s, 18H)
IR (cm^{-1}) 3430, 3340, 2880, 1640, 1560, 1440, 1240, 750

Example 37

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1,2,3,4-tetrahydro-1-naphthyl)urea

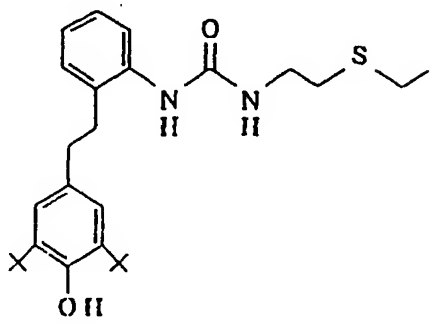


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1,2,3,4-tetrahydro-1-naphthylamine instead of decylamine. m.p. 168-169°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.01-7.27(m, 8H), 6.77(s, 2H), 5.08(s, 1H), 5.01-5.06(m, 2H), 4.42(d, J=8Hz, 1H), 2.65-2.90(m, 6H), 1.50-2.10(m, 4H), 1.35(s, 18H)
IR (cm^{-1}) 3650, 3350, 2960, 1640, 1560, 1440, 1240

Example 38

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(2-ethylthioethyl)urea



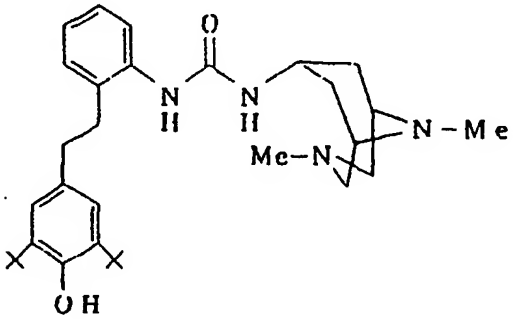
The title compound was prepared in a similar manner to that mentioned in Example 11, using 2-ethylthioethylamine instead of decylamine.

m.p. 131-132°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.19-7.28(m, 4H), 6.78(s, 2H), 5.12(s, 1H), 5.03(s, 1H), 4.63(t, J=6Hz, 1H), 3.33(dt, J=6, 7Hz, 2H), 2.80-2.85(m, 4H), 2.60(t, J=7Hz, 2H), 2.48(q, J=7Hz, 2H), 1.38(s, 18H), 1.20(t, J=7Hz, 3H)
IR (cm^{-1}) 3570, 3320, 2950, 2920, 1640, 1570, 1440, 1250, 1240

Example 39

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(3,9-dimethyl-3,9-diazabicyclo[3.3.1]-7-nonyl)urea

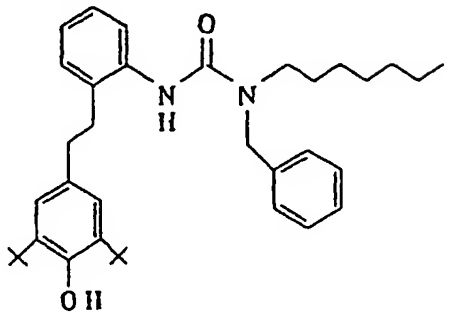


The title compound was prepared in a similar manner to that mentioned in Example 11, using 7-amino-3,9-dimethyl-3,9-diazabicyclo[3.3.1]nonane instead of decylamine.

^{1}H-NMR (δ ppm, $CDCl_3$) 8.55(d, J=10Hz, 1H), 7.14-7.27(m, 4H), 6.85(s, 2H), 5.14(s, 1H), 5.09(s, 1H), 4.10-4.26(m, 1H), 2.87-2.90(m, 2H), 2.77-2.80(m, 2H), 2.70(bs, 2H), 2.41(s, 3H), 2.19-2.38(m, 7H), 1.39(s, 18H), 1.23-1.37(m, 4H)
IR(cm^{-1}) 3638, 2926, 1651, 1509, 1435, 1377, 733

Example 40

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-benzyl-N'-heptylurea

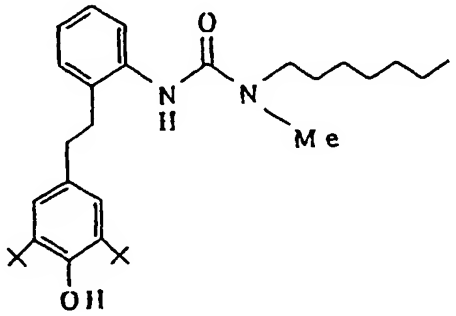


The title compound was prepared in a similar manner to that mentioned in Example 11, using N-heptylbenzylamine instead of decylamine.

^{1}H-NMR (δ ppm, $CDCl_3$) 7.7-7.75(m, 1H), 6.9-7.3(m, 8H), 6.78(s, 2H), 5.96(s, 1H), 5.06(s, 1H), 4.49(s, 2H), 3.30(t, J=8Hz, 2H), 2.65-2.69(m, 2H), 2.51-2.54(m, 2H), 1.59-1.63(m, 2H), 1.38(s, 18H), 1.22-1.28(m, 8H), 0.86(t, J=7Hz, 3H)
IR (cm^{-1}) 3640, 2960, 2940, 2870, 1660, 1530, 1460, 1440, 1240, 760

Example 41

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-heptyl-N'-methylurea

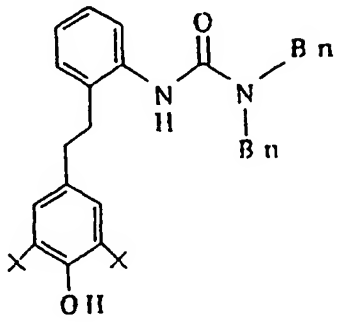


The title compound was prepared in a similar manner to that mentioned in Example 11, using N-methylheptylamine instead of decylamine.

^{1}H-NMR (δ ppm, $CDCl_3$) 7.36(d, J=8Hz, 1H), 7.18-7.22(m, 2H), 7.07-2.10(m, 1H), 6.81(s, 2H), 5.66(s, 1H), 5.08(s, 1H), 3.23(t, J=8Hz, 2H), 2.82(s, 4H), 2.71(s, 3H), 1.45-1.55(s, 2H), 1.36(s, 18H), 1.20-1.30(m, 8H), 0.86(t, J=7Hz, 3H)
IR (cm^{-1}) 2880, 2870, 2820, 1660, 1520, 1490, 1450, 1440, 1250, 760

Example 42

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N',N'-dibenzylurea

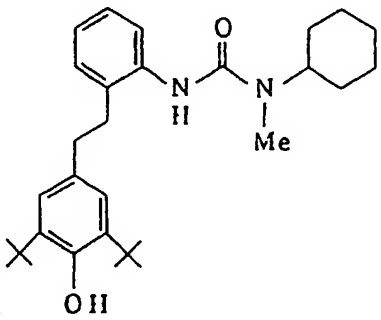


The title compound was prepared in a similar manner to that mentioned in Example 11, using N,N-dibenzylamine instead of decylamine.

^{1}H-NMR (δ ppm, $CDCl_3$) 7.69(d, J=8Hz, 1H), 7.15-7.29(m, 10H), 7.00(m, 1H), 6.90(t, J=8Hz, 1H), 6.80(d, J=8Hz, 1H), 6.74(s, 2H), 6.01(bs, 1H), 5.05(s, 1H), 4.54(s, 4H), 2.59(t, J=8Hz, 2H), 2.38(t, J=8Hz, 2H), 1.37(s, 18H)
IR (cm^{-1}) 3628, 3280, 2958, 1710, 1645, 1594, 1498, 1475, 1362, 1231, 754, 696

Example 43

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-cyclohexyl-N'-methylurea

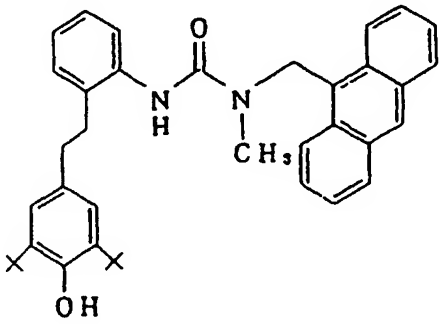


The title compound was prepared in a similar manner to that mentioned in Example 11, using N-methylcyclohexylamine instead of decylamine. Amorphous powders.

^{1}H-NMR (δ ppm, $CDCl_3$) 7.65(d, J=7Hz, 1H), 7.15-7.21(m, 2H), 7.06(t, J=7Hz, 1H), 6.81(s, 2H), 5.68(bs, 1H), 5.08(s, 1H), 4.13(m, 1H), 2.82(s, 4H), 2.54(s, 3H), 1.75-1.81(m, 2H), 1.60-1.75(m, 3H), 1.25-1.40(m, 23H)
IR (cm^{-1}) 3638, 3426, 2930, 1639, 1520, 1484, 1450, 1314, 1249, 1166, 1121, 751

Example 44

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(9-anthryl)methyl-N'-methylurea

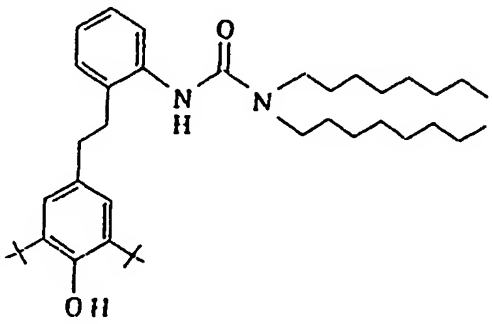


The title compound was prepared in a similar manner to that mentioned in Example 11, using 9-(methylaminomethyl)anthracene instead of decylamine.
m.p. 205-206°C

^{1}H-NMR (δ ppm, $CDCl_3$) 8.47(s, 1H), 8.37(d, J=9Hz, 2H), 8.02-8.04(m, 2H), 7.70(d, J=8Hz, 1H), 7.43-7.57(m, 4H), 7.15-7.31(m, 3H), 6.67(s, 2H), 5.67(s, 1H), 5.59(s, 2H), 4.94(s, 1H), 2.76-2.86(m, 4H), 2.34(s, 3H), 1.19(s, 18H)
IR (cm^{-1}) 3420, 2950, 1640, 1520, 1490, 1450, 1440, 1250, 740

Example 45

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N',N'-dioctylurea

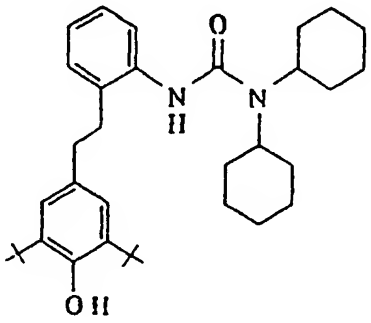


The title compound was prepared in a similar manner to that mentioned in Example 11, using N,N-dioctylamine instead of decylamine. m.p. 55-60°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.73(dd, J=8, 1Hz, 1H), 7.13-7.25(m, 2H), 7.00-7.05(m, 1H), 6.85(s, 2H), 5.94(s, 1H), 5.07(s, 1H), 3.18(t, J=8Hz, 4H), 2.81(s, 4H), 1.51-1.61(m, 4H), 1.39(s, 18H), 1.20-1.34(m, 20H), 0.87(t, J=7Hz, 6H)
IR (cm^{-1}) 3646, 3420, 3322, 1626, 1511

Example 46

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N',N'-dicyclohexylurea

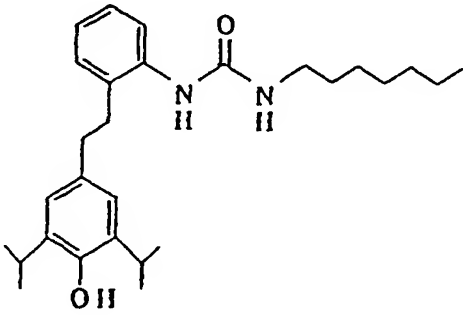


The title compound was prepared in a similar manner to that mentioned in Example 11, using N,N-dicyclohexylamine instead of decylamine.
m.p. 149-152°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.73(dd, J=8, 1Hz, 1H), 7.15-7.20(m, 1H), 7.13(dd, J=7, 2Hz, 1H), 7.00-7.05(m, 1H), 6.94(s, 2H), 6.15(s, 1H), 5.06(s, 1H), 3.42-3.52(m, 2H), 2.84(s, 4H), 1.55-1.83(m, 14H), 1.41(s, 18H), 1.22-1.34(m, 4H), 0.98-1.13(m, 2H)
IR (cm^{-1}) 3474, 3400, 1644, 1588, 1517

Example 47

N-[2-(3,5-diisopropyl-4-hydroxyphenethyl)phenyl]-N'-heptylurea



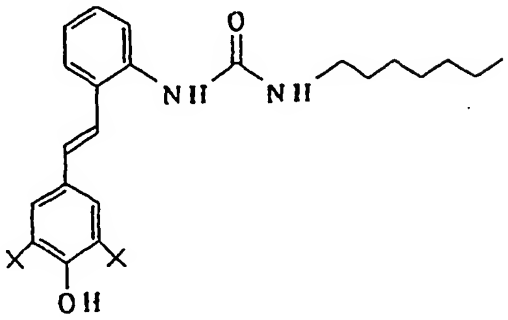
A solution of diphenylphosphoryl azide (0.88 g, 3.2 mmol), octanoic acid (0.42 g, 2.9 mmol) and triethylamine (0.32 g, 3.2 mmol) in toluene (10 ml) was stirred at room temperature for 1.5 hrs and further stirred at about 90°C for 2 hrs. After allowing the mixture to cool, a solution of 4-(2-aminophenethyl)-2,6-diisopropylphenol (0.85 g, 2.9 mmol) in toluene (2 ml) was added dropwise under ice-cooling while stirring. The reaction solution was returned slowly to room temperature and stirred overnight. The solvent was distilled off, the residue was purified by a silica gel column chromatography and recrystallized from ethyl acetate/hexane to give crystals of the title compound (0.99 g, 76%). m.p. 150-151°C

^{1}H-NMR (δ ppm, $CDCl_3$) 7.16-7.26(m, 4H), 6.69(s, 2H), 5.14(s, 1H), 4.73(s, 1H), 4.18(t, J=6Hz, 1H), 3.01-3.15(m,

4H), 2.71-2.89(m, 4H), 1.34-1.44(m, 2H), 1.2-1.3(m, 8H), 1.20,(s, 6H), 1.19(s, 6H), 0.86(t, J=7Hz, 3H)
IR (cm^{-1}) 3330, 2960, 2930, 1640, 1580, 1470, 1450, 1260, 750

Example 48

N-[2-(3,5-di-tert-butyl-4-hydroxystyryl)phenyl]-N'-heptylurea

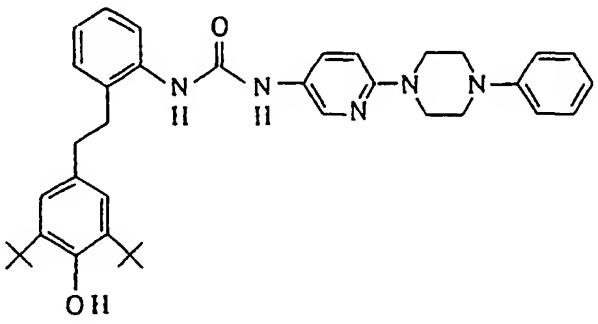


A solution of diphenylphosphoryl azide (0.36 g, 1.3 mmol), octanoic acid (0.17 g, 1.2 mmol) and triethylamine (0.13 g, 1.3 mmol) in toluene (5 ml) was stirred at room temperature for 1.5 hrs and further stirred at about 90°C for 2 hrs. After allowing the mixture to cool, a solution of 4-(2-aminostyryl)-2,6-di-tert-butylphenol (0.89 g, 1.2 mmol) in toluene (2 ml) was added dropwise under ice-cooling while stirring. The reaction solution was returned slowly to room temperature and stirred overnight. The solvent was distilled off, the residue was purified by a silica gel column chromatography and recrystallized from ethyl acetate/hexane to give crystals of the title compound (0.39 g, 70%). m.p. 162-164°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.63(dd, J=7, 2Hz, 1H), 7.33-7.37(m, 3H), 7.21-7.28(m, 2H), 7.08(d, J=16Hz, 1H), 7.01(d, J=16Hz, 1H), 6.01(bs, 1H), 5.33(s, 1H), 4.54(t, J=6Hz, 1H), 3.20(dt, J=6, 7Hz, 2H), 1.42-1.47(m, 20H), 1.20-1.36(m, 8H), 0.83(t, J=7Hz, 3H)
IR (cm^{-1}) 3626, 3334, 2954, 2926, 1642, 1568, 1454, 1439, 1235, 1152, 960, 751

Example 49

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[2-(4-phenyl-1-piperadinyl)-5-pyridyl]urea

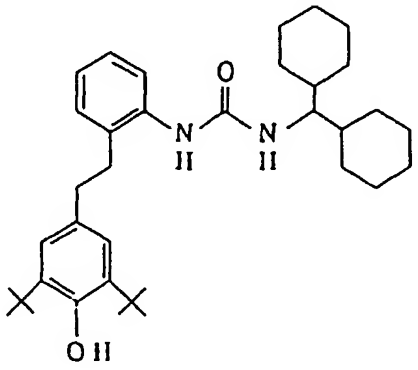


The title compound was prepared in a similar manner to that mentioned in Example 1, using 6-(4-phenyl-1-piperadinyl)nicotinic acid instead of 4-hexyloxybenzoic acid. m.p. 197-199°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.95(d, J=2Hz, 1H), 7.67(dd, J=9, 2Hz, 1H), 7.39(d, J=9Hz, 1H), 7.17-7.33(m, 5H), 6.94-7.00(m, 2H), 6.89(dd, J=7, 7Hz, 1H), 6.81(s, 2H), 6.65(d, J=9Hz, 1H), 5.85(bs, 1H), 5.22(bs, 1H), 5.16(s, 1H), 3.62(t, J=5Hz, 4H), 3.28(t, J=5Hz, 4H), 2.76-2.92(m, 4H), 1.38(s, 18H)
IR(cm^{-1}) 3620, 3330, 3290, 2954, 1646, 1600, 1547, 1492, 1233, 951, 760

Example 50

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(dicyclohexylmethyl)urea

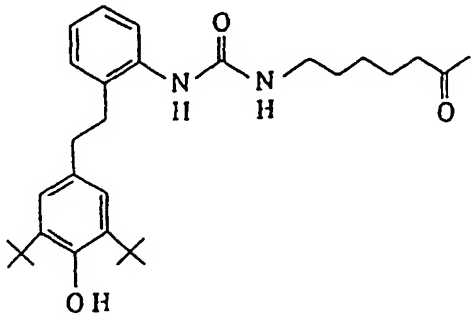


The title compound was prepared in a similar manner to that mentioned in Example 1, using dicyclohexylacetic acid instead of 4-hexyloxybenzoic acid.
m.p. 194-195°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.29-7.18(m, 4H), 6.81(s, 2H), 5.19(bs, 1H), 5.09(s, 1H), 4.00(d, J=10Hz, 1H), 3.47(bs, 1H), 2.88(t, J=7Hz, 2H), 2.80(t, J=7Hz, 2H), 1.54-1.70(m, 10H), 1.38(s, 18H), 1.38-1.42(m, 2H), 1.01-1.19(m, 8H), 0.73-0.80(m, 2H)
IR(cm^{-1}) 3642, 3362, 2924, 2852, 1641, 1553, 1436, 1235, 744

Example 51

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(6-oxoheptyl)urea

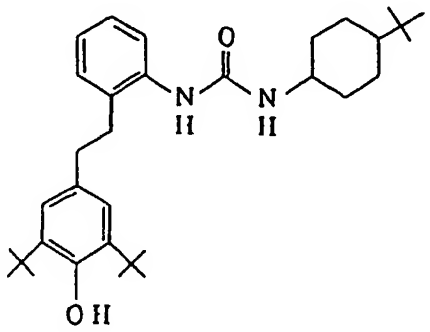


The title compound was prepared in a similar manner to that mentioned in Example 1, using 7-oxooctanoic acid instead of 4-hexyloxybenzoic acid. m.p. 73-76°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.16-7.25(m, 4H), 6.77(s, 2H), 5.12(s, 1H), 4.97(s, 1H), 4.17-4.24(m, 1H), 3.12(td, J=7, 6Hz, 2H), 2.76-2.86(m, 4H), 2.38(t, J=7Hz, 2H), 2.10(s, 3H), 1.49-1.57(m, 2H), 1.33-1.45(m, 4H), 1.37(s, 18H)
IR(cm^{-1}) 3368, 2950, 1712, 1632, 1574

Example 52

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-tert-butylcyclohexyl)urea

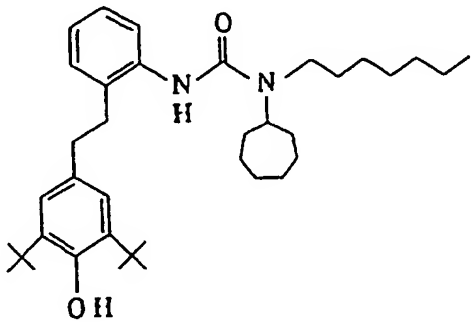


The title compound was prepared in a similar manner to that mentioned in Example 1, using 4-tert-butylcyclohexanecarboxylic acid instead of 4-hexyloxybenzoic acid. m.p. 206-208°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.15-7.25(m, 4H), 6.78(s, 2H), 5.10(s, 1H), 5.00(s, 1H), 4.02(d, J=8Hz, 1H), 3.47-3.57(m, 1H), 2.76-2.86(m, 4H), 1.96-1.98(m, 2H), 1.70-1.73(m, 2H), 1.38(s, 18H), 0.84-1.13(m, 5H), 0.81(s, 9H)
IR(cm^{-1}) 3642, 3356, 2948, 1640, 1585, 1436, 1234

Example 53

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-cycloheptyl-N'-heptylurea



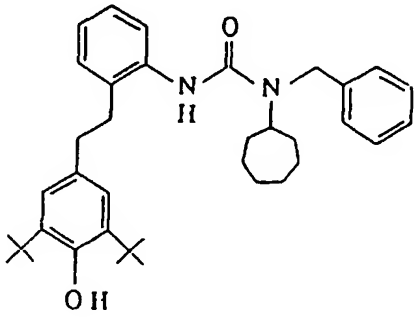
The title compound was prepared in a similar manner to that mentioned in Example 11, using N-heptylcycloheptylamine instead of decylamine. m.p. 70-72°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.77(dd, J=8, 1Hz, 1H), 7.20(ddd, J=8, 8, 2Hz, 1H), 7.13(dd, J=8, 1Hz, 1H), 7.02(ddd, J=8, 8, 1Hz, 1H), 6.89(s, 2H), 6.04(s, 1H), 5.06(s, 1H), 4.02(bs, 1H), 3.07-3.11(m, 2H), 2.82(s, 4H), 1.82-1.87(m, 2H), 1.58-1.70(m, 8H), 1.40-1.56(m, 4H), 1.40(s, 18H), 1.25(bs, 8H), 0.84-0.90(m, 3H)

IR(cm^{-1}) 3642, 3296, 2910, 1631, 1588, 1435, 1235, 751

Example 54

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-benzyl-N'-cycloheptylurea

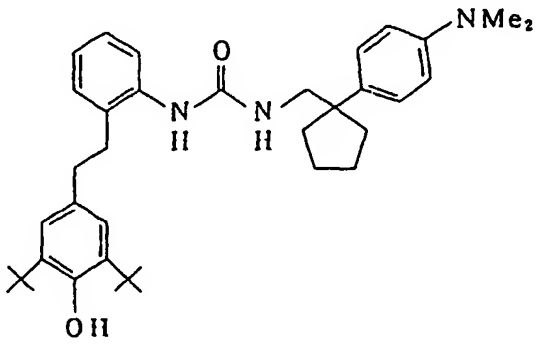


The title compound was prepared in a similar manner to that mentioned in Example 11, using benzylcycloheptylamine instead of decylamine. m.p. 183-184°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.74(d, J=8Hz, 1H), 7.25-7.30(m, 2H), 7.07-7.21(m, 4H), 6.90-6.93(m, 2H), 6.76(s, 2H), 5.95(s, 1H), 5.06(s, 1H), 4.42-4.50(m, 1H), 4.43(s, 2H), 2.52(t, J=8Hz, 2H), 2.23(t, J=8Hz, 2H), 1.92-1.99(m, 2H), 1.43-1.72(s, 10H), 1.42(s, 18H)
IR(cm^{-1}) 3638, 3402, 2926, 1671, 1589, 1527, 1455, 1232, 1213, 752

Example 55

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[[1-(4-dimethylaminophenyl)cyclopentyl]methyl]urea

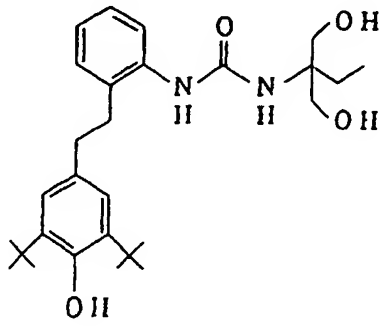


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-[1-(aminomethyl)cyclopentyl]-N,N-dimethylaniline instead of decylamine. m.p. 174-175°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.08-7.21(m, 3H), 7.03(d, J=7Hz, 1H), 6.92(d, J=9Hz, 2H), 6.77(s, 2H), 6.54(d, J=8Hz, 2H), 5.07(s, 2H), 4.07-4.15(m, 1H), 3.22(d, J=5Hz, 2H), 2.88(s, 6H), 2.69-2.79(m, 4H), 1.63-1.83(m, 8H), 1.36(s, 18H)
IR(cm^{-1}) 3640, 3360, 1644, 1525, 1435, 1233, 814, 749

Example 56

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(2-ethyl-1,3-dihydroxy-2-propyl)urea

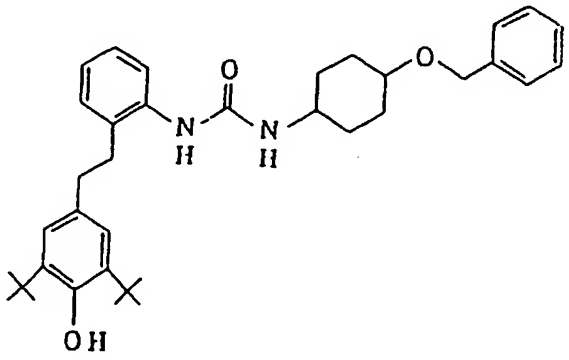


The title compound was prepared in a similar manner to that mentioned in Example 11, using 2-amino-2-ethyl-1,3-propanediol instead of decylamine. m.p. 145-146°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.16-7.31(m, 4H), 6.78(s, 2H), 5.12(s, 1H), 5.11(s, 1H), 4.61(s, 1H), 3.75-3.89(m, 4H), 3.46-3.55(m, 2H), 2.75-2.88(m, 4H), 1.51(q, J=8Hz, 2H), 1.38(s, 18H), 0.75(t, J=8Hz, 3H)
IR(cm^{-1}) 3640, 3570, 3400, 3340, 2970, 1660, 1610, 1560, 1440, 1250, 750, 650

Example 57

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-benzyloxycyclopropyl)urea

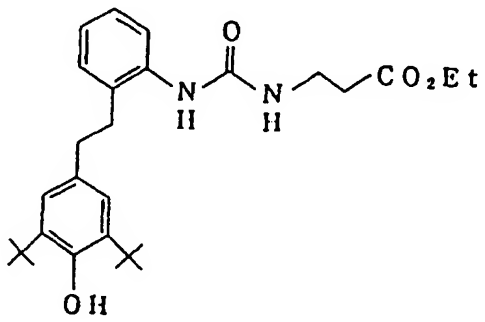


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-benzyloxycyclohexylamine instead of decylamine.
m.p. 152-153°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.16-7.36(m, 9H), 6.77(s, 2H), 5.11(s, 1H), 4.94(s, 1H), 4.51(s, 2H), 4.00(d, J=8Hz, 1H), 3.56-3.68(m, 1H), 3.18-3.28(m, 1H), 2.74-2.86(m, 4H), 1.93-2.15(m, 4H), 1.31-1.47(m, 2H), 1.38(s, 18H), 0.94-1.08(m, 2H)
IR(cm^{-1}) 3630, 3370, 3330, 2950, 1645, 1565, 1235, 1090, 750

Example 58

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(2-ethoxycarbonylethyl)urea

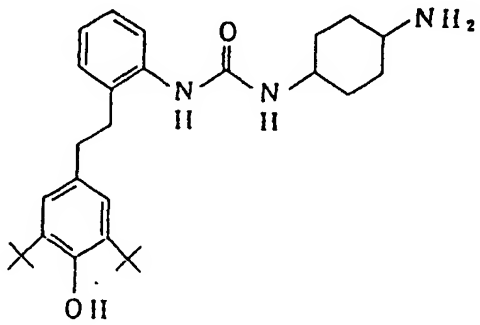


The title compound was prepared in a similar manner to that mentioned in Example 11, using ethyl 3-aminopropionate instead of decylamine. m.p. 158-159°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.14-7.28(m, 4H), 6.78(s, 2H), 5.12(s, 1H), 5.08(s, 1H), 4.75(t, J=6Hz, 1H), 4.07(q, J=7Hz, 2H), 3.41(dt, J=6, 6Hz, 1H), 2.74-2.86(m, 4H), 2.49(t, J=6Hz, 2H), 1.38(18H.s, 18H), 1.18(t, J=7Hz, 3H)
IR(cm^{-1}) 3630, 3320, 3270, 2960, 1730, 1630, 1570, 1440, 1235, 1190, 745

Example 59

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-aminocyclohexyl)urea

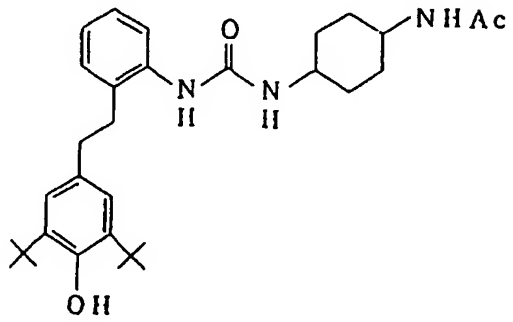


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1,4-diaminocyclohexane instead of decylamine.
m.p. >280°C (dec.)

^{1}H-NMR(δ ppm, $CDCl_3$) 7.14-7.28(m, 4H), 6.77(s, 2H), 5.12(bs, 1H), 4.97(bs, 1H), 3.98-4.05(m, 1H), 3.53-3.64(m, 1H), 2.74-2.87(m, 4H), 2.52-2.62(m, 1H), 1.89-1.97(m, 2H), 1.77-1.86(m, 2H), 1.38(s, 18H), 0.97-1.24(m, 4H)
IR(cm^{-1}) 3630, 3420, 3340, 2940, 1635, 1590, 1570, 1240, 935

Example 60

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-acetamidocyclohexyl)urea

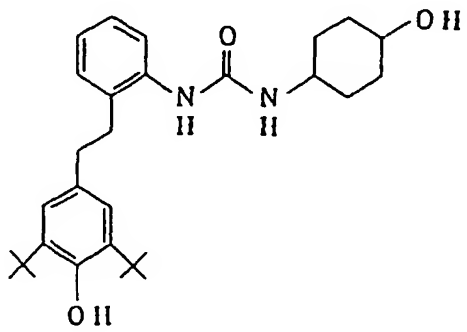


The title compound was prepared in a similar manner to that mentioned in Example 11, using N-(4-aminocyclohexyl)acetamide instead of decylamine.
m.p. 250°C (dec.)

^{1}H-NMR(δ ppm, $CDCl_3$) 7.16-7.30(m, 4H), 6.77(s, 2H), 5.26(bd, J=8Hz, 1H), 5.11(s, 1H), 4.93(s, 1H), 4.05(d, J=8Hz, 1H), 3.54-3.73(m, 2H), 2.74-2.87(m, 4H), 1.92-2.00(m, 4H), 1.93(s, 3H), 1.37(s, 18H), 1.03-1.27(m, 4H)
IR(cm^{-1}) 3640, 3290, 2950, 1635, 1550, 1440, 1235, 760

Example 61

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-hydroxycyclohexyl)urea

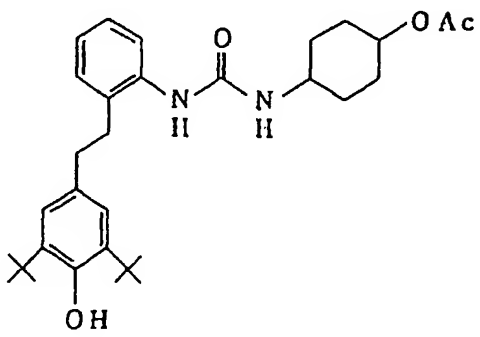


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-aminocyclohexanol instead of decylamine. m.p. 202-203°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.17-7.29(m, 4H), 6.77(s, 2H), 5.12(s, 1H), 4.94(s, 1H), 3.99(d, J=8Hz, 1H), 3.43-3.69(m, 2H), 2.75-2.87(m, 4H), 1.87-2.01(m, 4H), 1.28-1.43(m, 2H), 1.38(s, 18H), 0.97-1.12(m, 2H)
IR(cm^{-1}) 3645, 3320, 2950, 1640, 1570, 1440, 1235, 1070, 880, 745

Example 62

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-acetoxycyclohexyl)urea

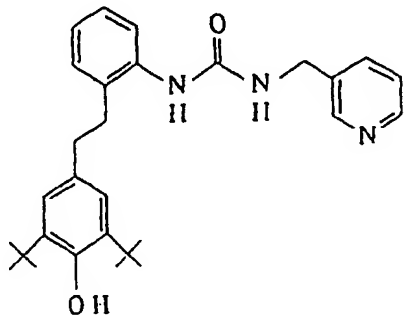


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-aminocyclohexyl acetate instead of decylamine. m.p. 92-94°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.17-7.28(m, 4H), 6.77(s, 2H), 5.12(s, 1H), 4.93(s, 1H), 4.53-4.64(m, 1H), 4.02(d, J=8Hz, 1H), 3.57-3.71(m, 1H), 2.78-2.87(m, 4H), 2.01(s, 3H), 1.87-2.02(m, 4H), 1.32-1.52(m, 2H), 1.38(s, 18H), 1.02-1.16(m, 2H)
IR(cm^{-1}) 3640, 3380, 2960, 1740, 1645, 1560, 1440, 1245, 1050, 765

Example 63

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(3-pyridylmethyl)urea

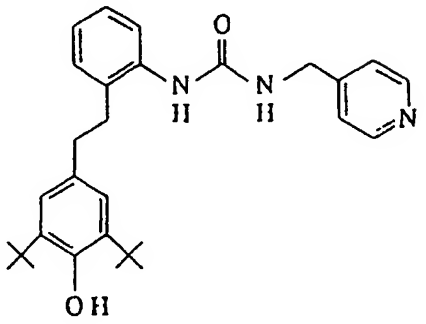


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3-(aminomethyl)pyridine instead of decylamine. m.p. 163-164°C

^{1}H-NMR(δ ppm, $CDCl_3$) 8.48(dd, J=5, 1Hz, 1H), 8.45(d, J=2Hz, 1H), 7.58(d, J=8Hz, 1H), 7.18-7.27(m, 5H), 6.75(s, 2H), 5.12(s, 1H), 4.95(s, 1H), 4.45-4.50(m, 1H), 4.34(d, J=6Hz, 2H), 2.75-2.86(m, 4H), 1.35(s, 18H)
IR(cm^{-1}) 3294, 1634, 1574, 1430, 1239, 1119, 760, 712

Example 64

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-pyridylmethyl)urea

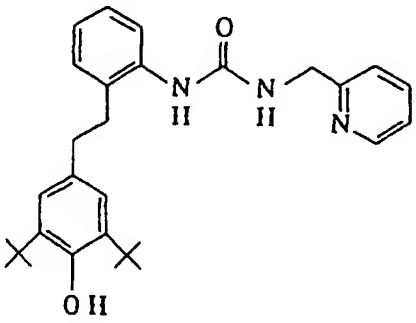


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-(aminomethyl)pyridine instead of decylamine. m.p. 214-215°C

^{1}H-NMR(δ ppm, $CDCl_3$) 8.50(dd, J=4, 1Hz, 2H), 7.30-7.25(m, 2H), 7.20-7.24(m, 2H), 7.12(d, J=6Hz, 2H), 6.77(s, 2H), 5.13(s, 1H), 5.00(s, 1H), 4.54(t, J=6Hz, 1H), 4.34(d, J=6Hz, 2H), 2.86-2.90(m, 2H), 2.79-2.82(m, 2H), 1.35(s, 18H)
IR(cm^{-1}) 3292, 1632, 1573, 1436, 1237, 761

Example 65

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(2-pyridylmethyl)urea

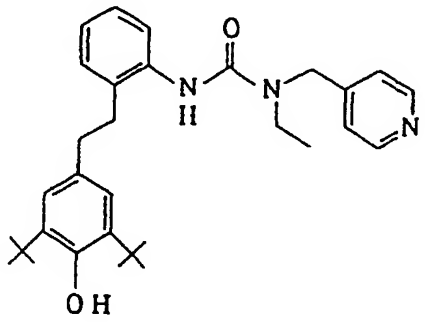


The title compound was prepared in a similar manner to that mentioned in Example 11, using 2-(aminomethyl)pyridine instead of decylamine. m.p. 189-190°C

^{1}H-NMR(δ ppm, $CDCl_3$) 8.42(dd, J=4, 1Hz, 1H), 7.61(ddd, J=8, 8, 2Hz, 1H), 7.38(dd, J=8, 1Hz, 1H), 7.12-7.24(m, 5H), 6.80(s, 2H), 5.48(bs, 1H), 5.36(t, J=5Hz, 1H), 5.29(s, 1H), 4.47(d, J=6Hz, 2H), 2.78-2.89(m, 4H), 1.36(s, 18H)
IR(cm^{-1}) 3632, 3612, 3296, 1627, 1576, 1437, 1234, 755

Example 66

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-ethyl-N'-(4-pyridylmethyl)urea

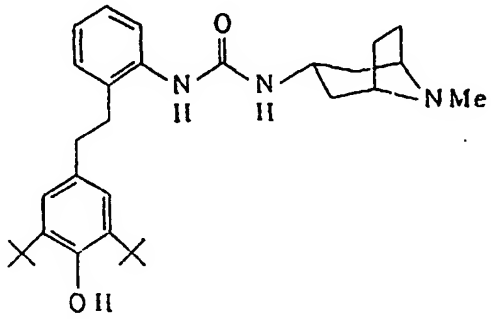


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-(ethylaminomethyl)pyridine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 8.51(dd, J=4, 1Hz, 2H), 7.66(dd, J=8, 1Hz, 1H), 7.09-7.25(m, 5H), 6.79(s, 2H), 5.85(s, 1H), 5.09(s, 1H), 4.50(s, 2H), 3.09(q, J=7Hz, 2H), 2.74-2.82(m, 4H), 1.36(s, 18H), 1.14(t, J=7Hz, 3H)
IR(cm^{-1}) 3266, 3060, 1630, 1606, 1516, 1492, 1451, 1431, 1269, 755, 746

Example 67

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(8-methyl-8-azabicyclo[3.2.1]-3-octyl)urea

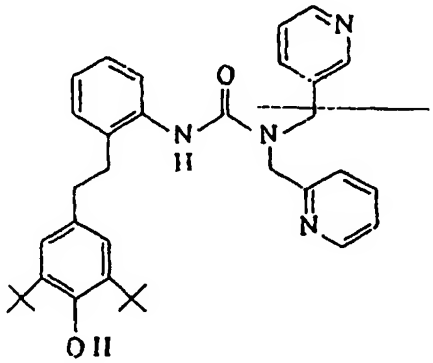


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3-amino-8-methyl-8-azabicyclo[3.2.1]octane instead of decylamine.
m.p. 229-230°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.27(d, J=4Hz, 1H), 7.13-7.21(m, 3H), 6.79(s, 2H), 5.51(bs, 1H), 5.14(s, 1H), 4.77(bs, 1H), 4.07-4.13(m, 1H), 3.51(bs, 2H), 2.76-2.87(m, 4H), 2.51(s, 3H), 2.13-2.15(m, 2H), 1.89-1.96(m, 6H), 1.38(m, 18H)
IR(cm^{-1}) 3360, 1645, 1565, 1435, 1240, 745

Example 68

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(2-pyridylmethyl)-N'-(3-pyridylmethyl)urea

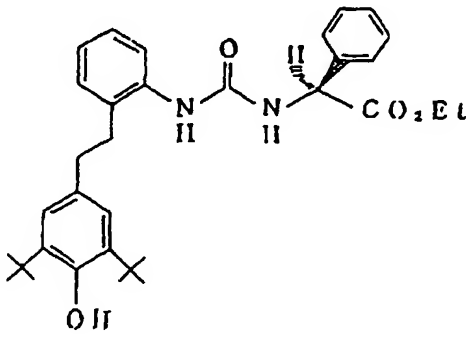


The title compound was prepared in a similar manner to that mentioned in Example 11, using N-(3-pyridylmethyl)-2-pyridylmethylamine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 9.47(s, 2H), 8.52(d, J=4Hz, 1H), 8.48(dd, J=5, 1Hz, 1H), 7.89(d, J=6Hz, 1H), 7.76(dd, J=8, 1Hz, 1H), 7.67(ddd, J=8, 8, 2Hz, 1H), 7.54(dd, J=8, 2Hz, 1H), 7.23(t, J=7Hz, 2H), 7.14-7.18(m, 1H), 7.02-7.06(m, 2H), 6.97(d, J=8Hz, 1H), 6.93(s, 2H), 5.19(s, 1H), 4.60(s, 2H), 4.37(s, 2H), 2.96-3.05(m, 2H), 2.90-2.94(m, 2H), 1.35(s, 18H)
IR(cm^{-1}) 3632, 3250, 1661, 1591, 1533, 1480, 1436, 1393, 1362, 1295, 1214, 755

Example 69

(S)-N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(α-ethoxycarbonyl)benzylurea

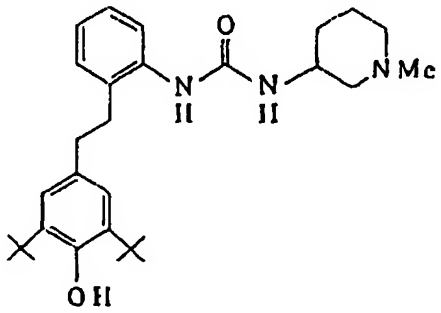


The title compound was prepared in a similar manner to that mentioned in Example 11, using (S)-α-phenylglycine ethyl ester instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.44(d, J=8Hz, 1H), 7.19-7.33(m, 8H), 6.78(s, 2H), 5.90(s, 1H), 5.74(d, J=7Hz, 1H), 5.59(d, J=8Hz, 1H), 5.16(s, 1H), 4.10-4.24(m, 2H), 2.89-2.92(m, 2H), 2.82-2.85(m, 2H), 1.43(s, 18H), 1.21(t, J=7Hz, 3H)
IR(cm^{-1}) 3636, 3294, 1737, 1643, 1542, 1435, 1233, 1181, 754

Example 70

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-methyl-3-piperidyl)urea

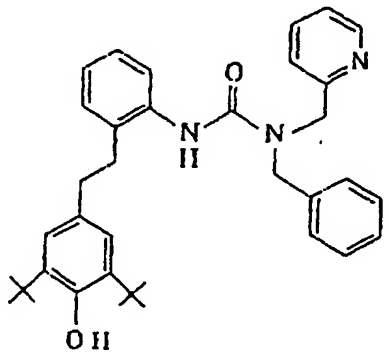


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3-amino-1-methylpiperidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.45(d, J=8Hz, 1H), 7.16-7.26(m, 3H), 6.92(s, 2H), 6.35(bs, 1H), 5.40(bs, 1H), 5.17(s, 1H), 3.45(bs, 1H), 3.18-3.23(m, 1H), 2.93-3.01(m, 1H), 2.83-2.92(m, 4H), 2.45-2.51(m, 1H), 2.34(s, 3H), 2.18-2.27(m, 1H), 1.82-1.95(m, 1H), 1.60-1.73(m, 3H), 1.46(s, 18H)
IR(cm^{-1}) 3638, 3250, 1643, 1548, 1436, 1235, 910, 733

Example 71

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-benzyl-N'-(2-pyridylmethyl)urea

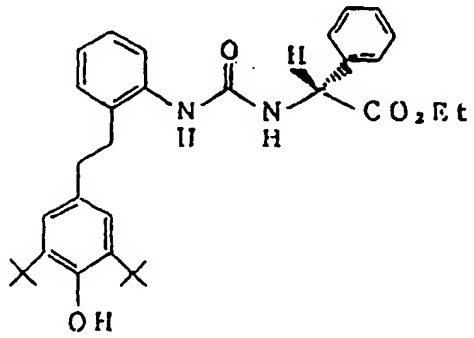


The title compound was prepared in a similar manner to that mentioned in Example 11, using N-benzyl-2-pyridylmethylamine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 9.20(bs, 1H), 7.92(d, J=4Hz, 1H), 7.78(d, J=7Hz, 1H), 7.52(ddd, J=8, 8, 2Hz, 1H), 7.19-7.30(m, 7H), 7.01-7.05(m, 2H), 6.93(s, 2H), 6.92-6.94(m, 1H), 5.06(s, 1H), 4.60(s, 2H), 4.41(s, 2H), 2.88-3.00(m, 4H), 1.36(s, 18H)
IR(cm^{-1}) 3620, 3250, 2244, 1657, 1590, 1532, 1453, 1436, 1213, 752, 732

Example 72

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(α-ethoxycarbonyl)benzylurea

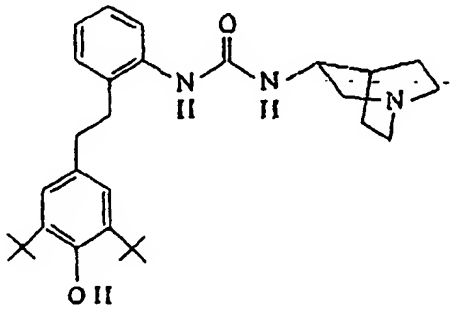


The title compound was prepared in a similar manner to that mentioned in Example 11, using (R)-α-phenylglycine ethyl ester instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.18-7.35(m, 9H), 6.77(s, 2H), 5.50(d, J=8Hz, 1H), 5.37(d, J=8Hz, 1H), 5.33(s, 1H), 5.09(s, 1H), 4.07-4.18(m, 2H), 2.78-2.84(m, 4H), 1.35(s, 18H), 1.17(t, J=7Hz, 3H)
IR(cm^{-1}) 3636, 3330, 1739, 1640, 1542, 1436, 1234, 1180, 935, 751, 698

Example 73

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-azabicyclo[2.2.2]-3-octyl)urea

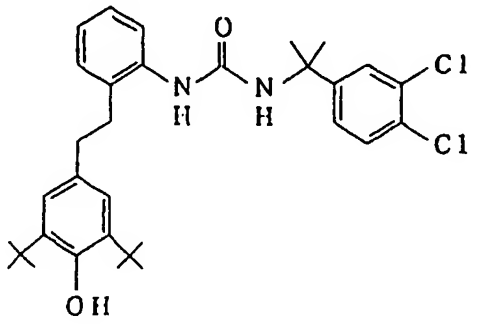


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3-amino-1-azabicyclo[2.2.2]octane instead of decylamine.
m.p. 227-229°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.21-7.27(m, 4H), 6.77(s, 2H), 5.11(s, 1H), 5.07(s, 1H), 4.43(d, J=7Hz, 1H), 3.78-3.85(m, 1H), 3.28(ddd, J=14, 10, 2Hz, 1H), 2.65-2.89(m, 8H), 2.29-2.33(m, 1H), 1.85-1.87(m, 1H), 1.55-1.70(m, 4H), 1.38(s, 18H)
IR(cm^{-1}) 3636, 3368, 3260, 1640, 1587, 1564, 1434, 1237, 1122, 765, 753

Example 74

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[2-(3,4-dichlorophenyl)-2-propyl]urea

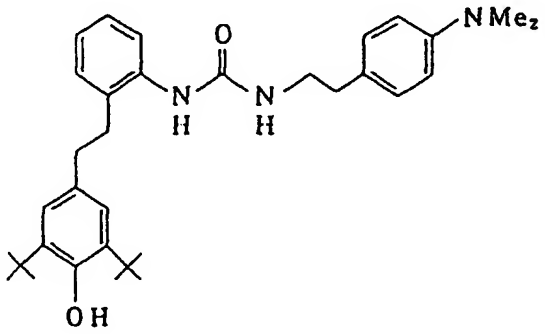


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3,4-dichloro-α,α-dimethylbenzylamine instead of decylamine.
m.p. 203-205°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.41(d, J=2Hz, 1H), 7.16-7.32(m, 6H), 6.81(s, 2H), 5.17(s, 1H), 5.11(s, 1H), 4.60(s, 1H), 2.79-2.83(m, 4H), 1.56(s, 6H), 1.39(s, 18H)
IR(cm^{-1}) 3638, 3352, 3282, 1644, 1564, 1558, 1437, 1235, 1171, 1030, 768, 745

Example 75

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-dimethylaminophenethyl)urea

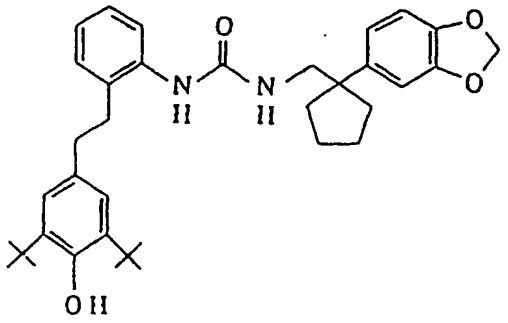


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-dimethylaminophenethylamine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.11-7.24(m, 4H), 6.96(d, J=9Hz, 2H), 6.77(s, 2H), 6.62(s, 2H), 5.09(s, 1H), 5.08(s, 1H), 4.03(t, J=6Hz, 1H), 3.33(td, J=7, 6Hz, 2H), 2.89(s, 6H), 2.72-2.86(m, 4H), 2.64(t, J=7Hz, 2H), 1.37(s, 18H)
IR(cm^{-1}) 3640, 3342, 2940, 1640, 1562, 1521, 1439, 1232, 660, 643

Example 76

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[[1-(3,4-methylenedioxyphenyl)cyclopentyl]methyl]urea

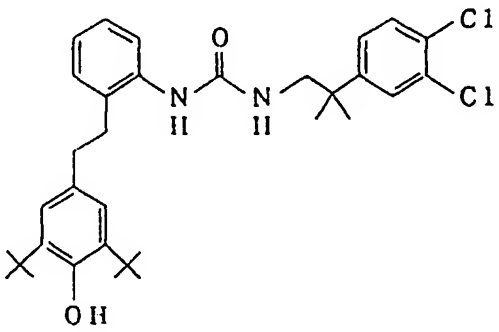


The title compound was prepared in a similar manner to that mentioned in Example 11, using 5-[1-(aminomethyl)cyclopentyl]-1,3-dioxaindane instead of decylamine. m.p. 188-189°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.12-7.22(m, 3H), 7.03(d, J=7Hz, 1H), 6.75(s, 2H), 6.59(d, J=2Hz, 1H), 6.57(d, J=8Hz, 1H), 6.47(dd, J=8, 2Hz, 1H), 5.88(s, 2H), 5.08(s, 1H), 5.00(s, 1H), 3.95-4.00(m, 1H), 3.21(d, J=5Hz, 2H), 2.70-2.80(m, 4H), 1.55-1.85(m, 8H), 1.36(s, 18H)
IR(cm^{-1}) 3640, 3388, 3328, 1645, 1561, 1488, 1435, 1363, 1234, 1042, 940, 760

Example 77

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[2-(3,4-dichlorophenyl)-2-methylpropyl]urea

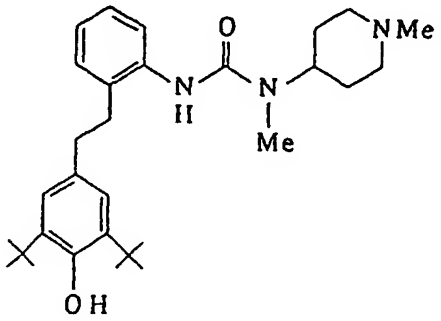


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3,4-dichloro-β,β-dimethylphenethylamine instead of decylamine.
m.p. 165-167°C

^{1}H-NMR(δ ppm, $CDCl_3$) 6.95-7.29(m, 7H), 6.73(s, 2H), 5.09(s, 1H), 4.90-5.00(m, 1H), 3.96(bs, 1H), 3.29(d, J=6Hz, 2H), 2.65-2.75(m, 4H), 1.35(s, 18H), 1.23(s, 6H)
IR(cm^{-1}) 3638, 3364, 1646, 1587, 1563, 1475, 1437, 1235, 762

Example 78

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-methyl-N'-(1-methyl-4-piperidyl)urea

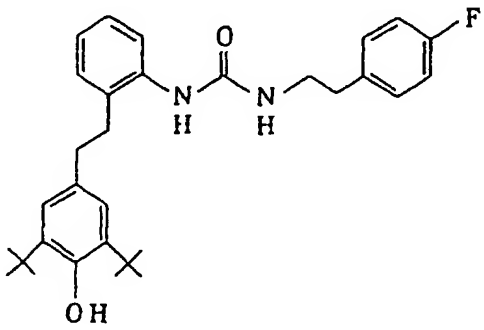


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-methyl-4-(methylamino)piperidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.63(d, J=7Hz, 1H), 7.19-7.26(m, 2H), 7.10(ddd, J=7, 7, 1Hz, 1H), 6.79(s, 2H), 5.63(s, 1H), 5.08(s, 1H), 4.20-4.27(m, 1H), 2.85-2.90(m, 2H), 2.82(s, 4H), 2.48(s, 3H), 2.28(s, 3H), 1.98-2.07(m, 2H), 1.55-1.90(m, 4H), 1.35(s, 18H)
IR(cm^{-1}) 3424, 1638, 1511, 1484, 1450, 1436, 1287, 1042, 754

Example 79

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-fluorophenethyl)urea

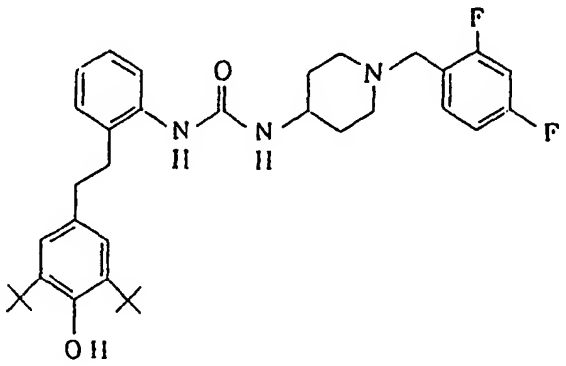


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-fluorophenethylamine instead of decylamine. m.p. 177-179°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.03-7.26(m, 6H), 6.89-6.93(m, 2H), 6.76(m, 2H), 5.10(s, 1H), 4.94(s, 1H), 4.15-4.20(m, 1H), 3.35(q, J=7Hz, 2H), 2.76-2.82(m, 4H), 2.71(t, J=7Hz, 2H), 1.36(s, 18H)
IR(cm^{-1}) 3636, 3348, 1643, 1563, 1511, 1438, 1234, 831, 747

Example 80

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(2,4-difluorobenzyl)-4-pyperidyl]urea

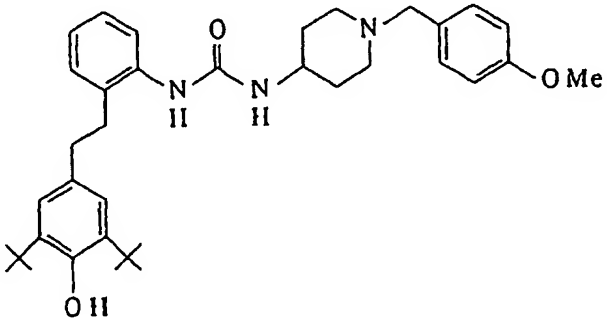


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-(2,4-difluorobenzyl)pyperidine instead of decylamine.
m.p. 157-158°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.15-7.36(m, 5H), 6.89-6.72(m, 4H), 5.11(s, 1H), 4.97(s, 1H), 4.09(d, J=8Hz, 1H), 3.57-3.72(m, 1H), 3.47(s, 2H), 2.68-2.88(m, 6H), 2.14-2.20(m, 2H), 1.82-1.95(m, 2H), 1.58-1.74(m, 2H), 1.20-1.40(m, 2H), 1.37(s, 18H)
IR(cm^{-1}) 3640, 3370, 3250, 2960, 1690, 1650, 1590, 1565, 1505, 1235, 850, 760

Example 81

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(4-methoxybenzyl)-4-piperidyl]urea

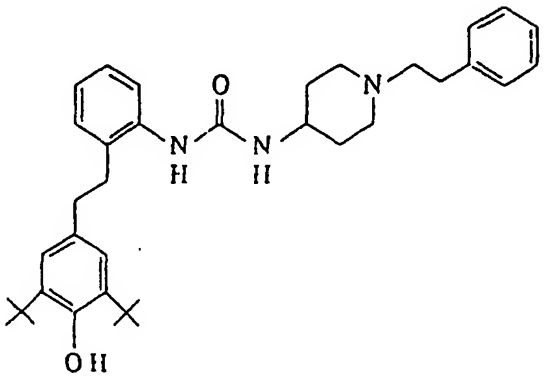


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-(4-methoxybenzyl)piperidine instead of decylamine.
m.p. 152-153°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.14-7.30(m, 6H), 6.74-6.88(m, 4H), 5.11(s, 1H), 4.97(s, 1H), 4.09(d, J=8Hz, 1H), 3.79(s, 3H), 3.56-3.72(m, 1H), 3.38(s, 2H), 2.67-2.88(m, 6H), 1.96-2.09(m, 2H), 1.82-1.92(m, 2H), 1.37(s, 18H), 1.18-1.35(m, 2H)
IR(cm^{-1}) 3640, 3360, 3260, 2950, 1645, 1595, 1565, 1515, 1245, 1045, 760

Example 82

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-phenethyl-4-piperidyl)urea

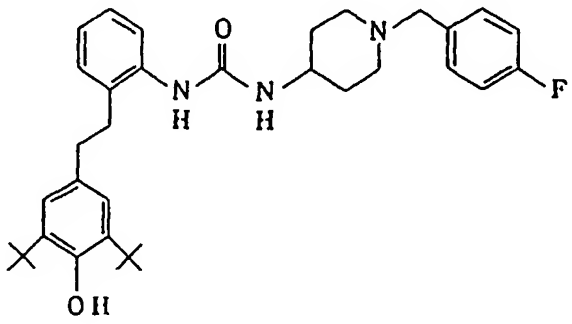


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-phenethylpiperidine instead of decylamine. m.p. 175-176°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.15-7.31(m, 9H), 6.78(s, 2H), 5.12(s, 1H), 5.01(s, 1H), 4.13(d, J=8Hz, 1H), 3.58-3.73(m, 1H), 2.72-2.91(m, 8H), 2.50-2.57(m, 2H), 2.05-2.16(m, 2H), 1.38(s, 18H), 1.24-1.35(m, 2H)
IR(cm^{-1}) 3640, 3340, 2950, 1640, 1590, 1565, 1435, 1235, 770, 750, 700

Example 83

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(4-fluorobenzyl)-4-piperidyl]urea

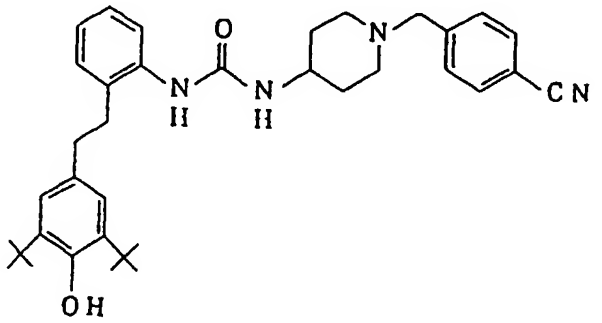


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-(4-fluorobenzyl)piperidine instead of decylamine.
m.p. 174-175°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.16-7.29(m, 6H), 6.93-7.00(m, 2H), 6.77(s, 2H), 5.11(s, 1H), 4.97(s, 1H), 4.09(d, J=8Hz, 1H), 3.57-3.71(m, 1H), 3.39(s, 2H), 2.66-2.87(m, 6H), 1.98-2.08(m, 2H), 1.82-1.90(m, 2H), 1.37(s, 18H), 1.22-1.34(m, 2H)
IR(cm^{-1}) 3645, 3370, 2950, 1540, 1590, 1560, 1510, 1225, 750

Example 84

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(4-cyanobenzyl)-4-piperidyl]urea

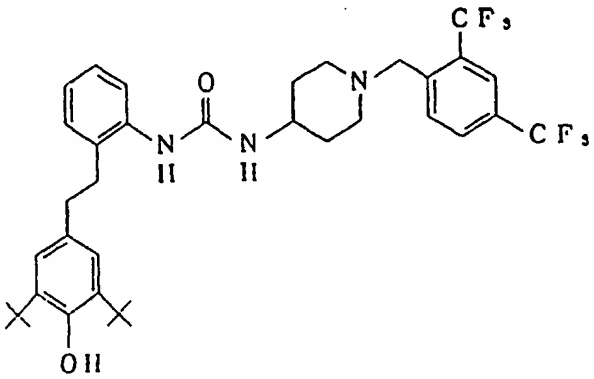


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-(4-cyanobenzyl)piperidine instead of decylamine. m.p. 197-198°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.58(d, J=8Hz, 2H), 7.40(d, J=8Hz, 2H), 7.17-7.29(m, 4H), 6.77(s, 2H), 5.12(s, 1H), 4.97(s, 1H), 4.10(d, J=8Hz, 1H), 3.59-3.72(m, 1H), 3.48(s, 2H), 2.75-2.87(m, 4H), 2.64-2.73(m, 2H), 2.03-2.13(m, 2H), 1.83-1.91(m, 2H), 1.37(s, 18H), 1.23-1.35(m, 2H)
IR(cm^{-1}) 3580, 3355, 3250, 2960, 2240, 1645, 1590, 1560, 1235, 825, 765, 550

Example 85

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-[2,4-bis(trifluoromethyl)benzyl]-4-piperidyl]urea

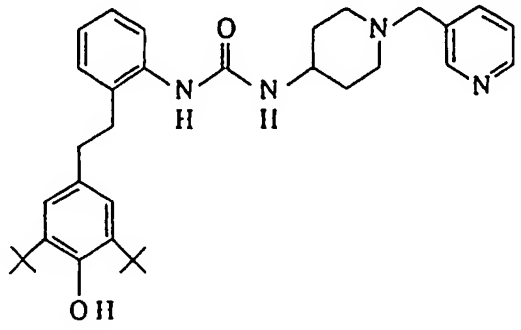


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-[2,4-bis(trifluoromethyl)benzyl]piperidine instead of decylamine. m.p. 156-157°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.92(d, J=8Hz, 1H), 7.85(s, 1H), 7.73(d, J=8Hz, 1H), 7.17-7.29(m, 4H), 6.78(s, 2H), 5.12(s, 1H), 4.98(s, 1H), 4.11(d, J=8Hz, 1H), 3.61-3.74(m, 1H), 3.64(s, 2H), 2.75-2.88(m, 4H), 2.64-2.73(m, 2H), 2.13-2.23(m, 2H), 1.84-1.92(m, 2H), 1.38(s, 18H), 1.27-1.36(m, 2H)
IR(cm^{-1}) 3645, 3350, 2955, 1600, 1565, 1440, 1350, 1280, 1175, 1130, 1060, 750, 680

Example 86

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(3-pyridylmethyl)-4-piperidyl]urea

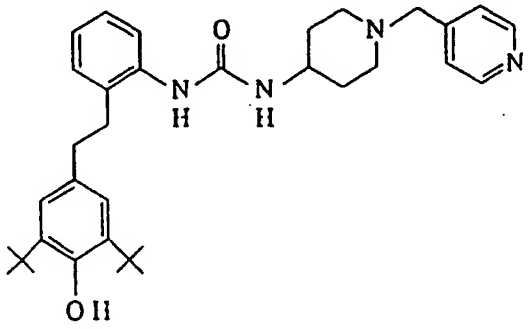


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-(3-pyridylmethyl)piperidine instead of decylamine.
m.p. 156-158°C

^{1}H-NMR(δ ppm, $CDCl_3$) 8.46-8.52(m, 2H), 7.60(d, J=8Hz, 1H), 7.16-7.28(m, 5H), 6.77(s, 2H), 5.12(s, 1H), 5.02(s, 1H), 4.13(d, J=8Hz, 1H), 3.58-3.72(m, 1H), 3.45(s, 2H), 2.67-2.87(m, 6H), 2.03-2.12(m, 2H), 1.82-1.90(m, 2H), 1.37(s, 18H), 1.22-1.37(m, 2H)
IR(cm^{-1}) 3632, 3362, 2950, 1645, 1561, 1433, 1232, 759, 713

Example 87

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(4-pyridylmethyl)-4-piperidyl]urea

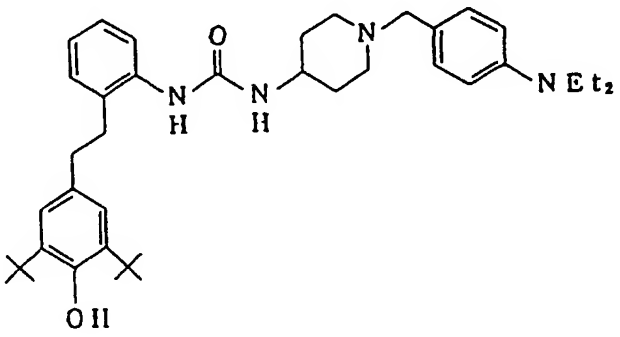


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-(4-pyridylmethyl)piperidine instead of decylamine.
m.p. 156-158°C

^{1}H-NMR(δ ppm, $CDCl_3$) 8.51(dd, J=4, 2Hz, 2H), 7.16-7.28(m, 6H), 6.77(s, 2H), 5.12(s, 1H), 5.00(s, 1H), 4.12(d, J=8Hz, 1H), 3.60-3.72(m, 1H), 3.44(s, 2H), 2.74-2.88(m, 4H), 2.66-2.74(m, 2H), 2.04-2.14(m, 2H), 1.83-1.92(m, 2H), 1.38(s, 18H), 1.25-1.38(m, 2H)
IR(cm^{-1}) 3630, 3292, 2948, 1620, 1560, 1435, 1237, 1109, 759

Example 88

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(4-diethylaminobenzyl)-4-piperidyl]urea

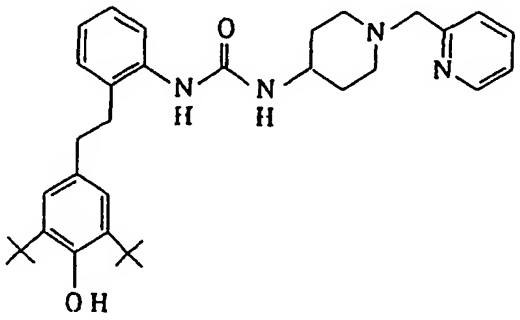


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-(4-diethylaminobenzyl)piperidine instead of decylamine.
m.p. 138-141°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.16-7.27(m, 4H), 7.09(d, J=8Hz, 2H), 6.77(s, 2H), 6.60(d, J=8Hz, 2H), 5.11(s, 1H), 4.99(s, 1H), 4.12(bd, J=7Hz, 1H), 3.58-3.70(m, 1H), 3.28-3.40(m, 6H), 2.73-2.86(m, 6H), 1.98-2.08(m, 2H), 1.82-1.89(m, 2H), 1.37(s, 18H), 1.25-1.37(m, 2H), 1.14(t, J=7Hz, 6H)
IR(cm^{-1}) 3630, 3410, 2950, 1641, 1553, 1520, 1232, 758

Example 89

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(2-pyridylmethyl)-4-piperidyl]urea

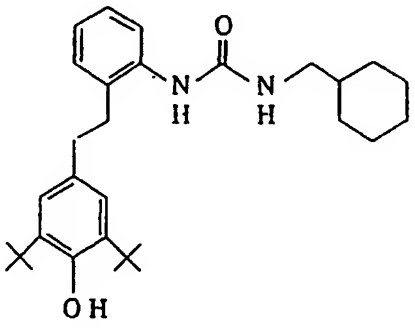


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-(2-pyridylmethyl)piperidine instead of decylamine.
m.p. 106-109°C

^{1}H-NMR(δ ppm, $CDCl_3$) 8.54(d, J=4Hz, 1H), 7.58-7.65(m, 1H), 7.33(d, J=8Hz, 1H), 7.12-7.27(m, 6H), 6.77(s, 2H), 5.11(s, 1H), 5.01(s, 1H), 4.14(d, J=7Hz, 1H), 3.61-3.73(m, 1H), 3.59(s, 2H), 2.70-2.86(m, 6H), 2.12-2.21(m, 2H), 1.83-1.91(m, 2H), 1.37(s, 18H), 1.30-1.42(m, 2H)
IR(cm^{-1}) 3630, 3330, 2948, 1639, 1589, 1543, 1436, 1233, 1121, 756

Example 90

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(cyclohexylmethyl)urea

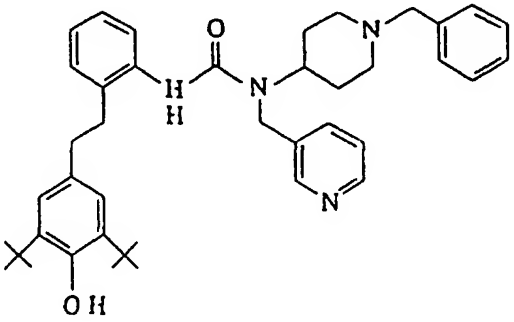


The title compound was prepared in a similar manner to that mentioned in Example 11, using aminomethylcyclohexane instead of decylamine. m.p. 208-210°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.18-7.24(m, 4H), 6.78(s, 2H), 5.11(s, 1H), 4.98(bs, 1H), 4.18-4.28(m, 1H), 2.97(t, J=6Hz, 2H), 2.74-2.90(m, 4H), 1.55-1.70(m, 5H), 1.38(s, 18H), 1.08-1.30(m, 4H), 0.78-0.90(m, 2H)
IR(cm^{-1}) 3616, 3304, 2922, 1627, 1579, 1435, 1233

Example 91

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-benzyl-4-pyperidyl)-N'-(3-pyridylmethyl)urea

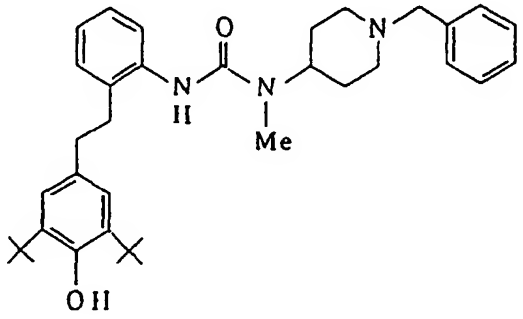


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-benzyl-4-(3-pyridylmethylamino)piperidine instead of decylamine.
m.p. 127-130°C

^{1}H-NMR(δ ppm, $CDCl_3$) 8.55(d, J=2Hz, 1H), 8.41(dd, J=5, 2Hz, 1H), 7.65(d, J=8Hz, 1H), 7.59(d, J=8Hz, 1H), 7.13-7.30(m, 6H), 7.18(m, 1H), 7.10(dd, J=8, 5Hz, 1H), 7.01(d, J=4Hz, 2H), 6.75(s, 2H), 5.90(bs, 1H), 5.11(s, 1H), 4.45(s, 2H), 4.22-4.33(m, 1H), 3.47(s, 2H), 2.86-2.97(m, 2H), 2.61(t, J=7Hz, 2H), 2.44(t, J=7Hz, 2H), 2.00-2.14(m, 2H), 1.60-1.86(m, 4H), 1.38(s, 18H)
IR(cm^{-1}) 3450, 3290, 1628, 1512, 1264, 1121, 1029, 742

Example 92

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-benzyl-4-piperidyl)-N'-methylurea

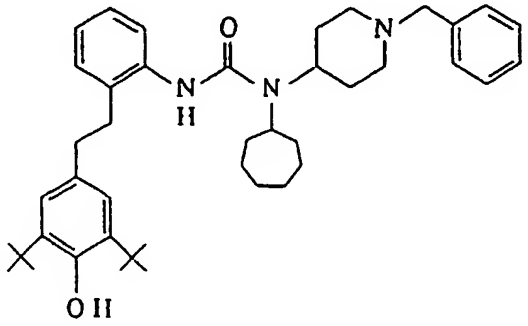


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-benzyl-4-(methylamino)piperidine instead of decylamine.
m.p. 144-146°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.62(d, J=8Hz, 1H), 7.10-7.30(m, 7H), 7.10(d, J=7Hz, 1H), 6.78(s, 2H), 5.62(bs, 1H), 5.08(s, 1H), 4.23(s, 1H), 3.48(s, 2H), 2.86-2.98(m, 2H), 2.81(s, 4H), 2.50(s, 3H), 1.98-2.10(m, 2H), 1.50-1.70(m, 4H), 1.35(s, 18H)
IR(cm^{-1}) 3328, 2954, 1632, 1512, 1196, 1041, 755, 701

Example 93

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-benzyl-4-piperidyl)-N'-cycloheptylurea

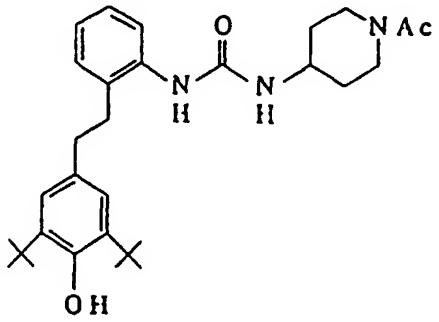


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-benzyl-4-(cycloheptylamino)piperidine instead of decylamine.
m.p. 107-109°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.72(d, J=8Hz, 1H), 7.23-7.36(m, 5H), 7.19(t, J=7Hz, 1H), 7.13(d, J=6Hz, 1H), 7.02(t, J=7Hz, 1H), 6.93(s, 2H), 6.12(bs, 1H), 5.05(s, 1H), 4.04-4.154(m, 1H), 3.49(s, 2H), 3.37-3.50(m, 1H), 2.90-3.00(m, 2H), 2.84(s, 4H), 1.97-2.10(m, 4H), 1.78-1.89(m, 4H), 1.20-1.65(m, 28H)
IR(cm^{-1}) 3476, 2922, 1662, 1528, 1454, 1236, 753

Example 94

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-acetyl-4-piperidyl)urea

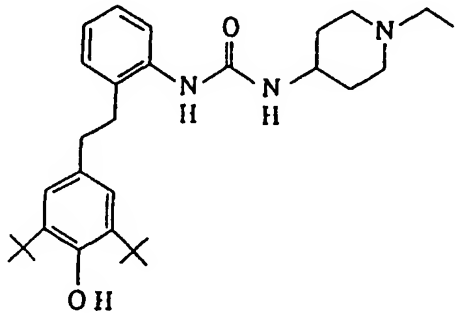


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-acetyl-4-aminopiperidine instead of decylamine. m.p. 218-221°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.15-7.29(m, 4H), 6.76(s, 2H), 5.13(s, 1H), 4.93(bs, 1H), 4.43-4.52(m, 1H), 4.05-4.13(m, 1H), 3.76-3.90(m, 1H), 3.66-3.73(m, 1H), 3.04-3.14(m, 1H), 2.71-2.85(m, 4H), 2.58-2.70(m, 1H), 2.05(s, 3H), 1.95-2.06(m, 1H), 1.82-1.90(m, 1H), 1.37(s, 18H), 1.10-1.20(m, 2H)
IR(cm^{-1}) 3302, 2952, 1629, 1561, 1434, 1234

Example 95

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-ethyl-4-piperidyl)urea

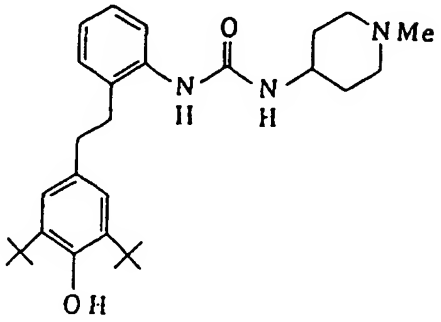


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-ethylpiperidine instead of decylamine. m.p. 182-184°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.10-7.30(m, 4H), 6.77(s, 2H), 5.11(s, 1H), 5.00(bs, 1H), 4.14(bd, J=8Hz, 1H), 3.58-3.72(m, 1H), 2.70-2.90(m, 6H), 2.39(q, J=7Hz), 1.97-2.12(m, 2H), 1.85-1.97(m, 2H), 1.37(s, 18H), 1.30-1.40(m, 2H), 1.07(t, J=7Hz, 3H)
IR(cm^{-1}) 3362, 2950, 1640, 1563, 1435, 1235

Example 96

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-methyl-4-piperidyl)urea

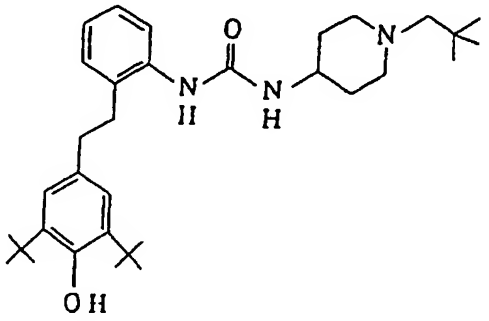


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-methylpiperidine instead of decylamine. m.p. 193-195°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.15-7.25(m, 4H), 6.77(s, 2H), 5.12(s, 1H), 4.97(bs, 1H), 4.10(bd, J=8Hz, 1H), 3.58-3.70(m, 1H), 2.70-2.85(m, 6H), 2.25(s, 3H), 2.02-2.12(m, 2H), 1.84-1.93(m, 2H), 1.38(s, 18H), 1.30-1.43(m, 2H)
IR(cm^{-1}) 3360, 2944, 1639, 1562

Example 97

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(2,2-dimethylpropyl)-4-piperidyl]urea

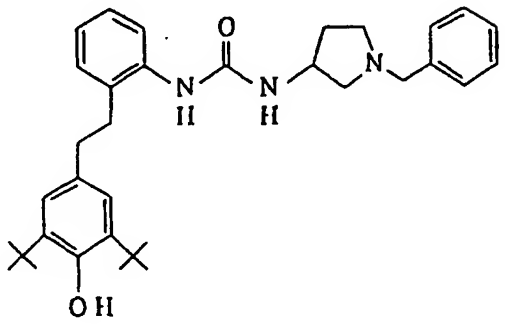


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-(2,2-dimethylpropyl)piperidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.18-7.26(m, 4H), 6.78(s, 2H), 5.11(s, 1H), 5.06(bs, 1H), 4.12(bd, J=8Hz, 1H), 3.53-3.65(m, 1H), 2.75-2.90(m, 4H), 2.60-2.68(m, 2H), 2.22-2.32(m, 2H), 1.98(s, 2H), 1.73-1.83(m, 2H), 1.38(s, 18H), 1.20-1.40(m, 2H), 0.81(s, 9H)
IR(cm^{-1}) 3322, 2952, 1638, 1536, 1435, 1234

Example 98

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-benzyl-3-pyrrolidinyl)urea

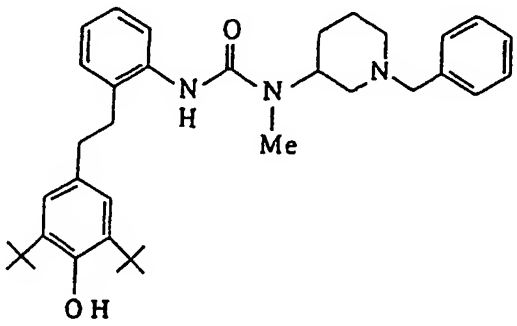


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3-amino-1-benzylpyrrolidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.10-7.30(m, 9H), 6.78(s, 2H), 5.37(bs, 1H), 5.10(s, 1H), 4.71(bd, J=8Hz, 1H), 4.23-4.34(m,1H), 3.55(d, J=13Hz, 1H), 3.50(d, J=13Hz, 1H), 2.70-2.81(m, 6H), 2.49(d, J=4Hz, 2H), 2.14-2.36(m, 2H), 1.37(s, 18H)
IR(cm^{-1}) 3634, 3304, 2954, 1638, 1559, 1436, 1234, 749, 699

Example 99

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-benzyl-3-piperidyl)-N'-methylurea

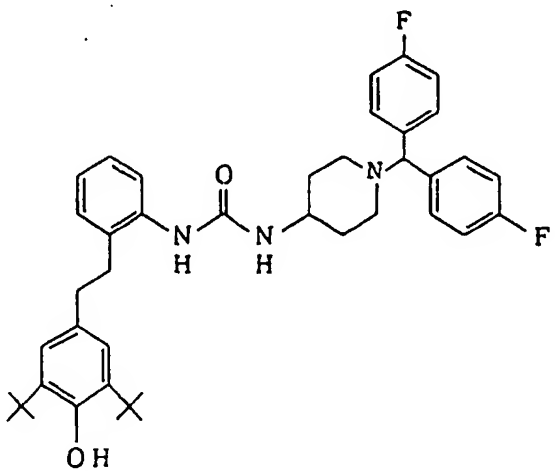


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3-amino-1-benzylpiperazine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.59(d, J=8Hz, 1H), 7.15-7.40(m, 7H), 7.08(t, J=7Hz, 1H), 6.79(s, 2H), 5.72(bs, 1H), 5.06(s, 1H), 4.22-4.34(m, 1H), 3.48(s, 2H), 2.70-2.80(m, 6H), 2.58(s, 3H), 1.60-1.90(m, 4H), 1.30-1.46(m, 2H), 1.35(s, 18H)
IR(cm^{-1}) 3630, 3422, 2940, 1639, 1520, 1485, 1452, 1312, 1249, 1122, 752, 699

Example 100

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-[bis(4-fluorophenyl)methyl]-4-piperidyl]urea

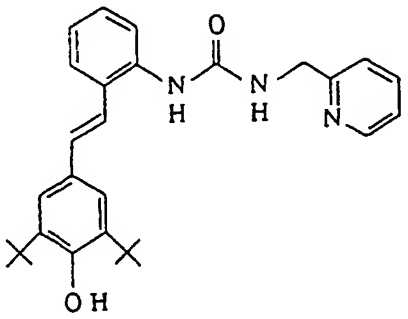


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-[bis(4-fluorophenyl)methyl]piperidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.65-7.80(m, 4H), 7.15-7.30(m, 4H), 7.12(t, J=7Hz, 2H), 6.84(d, J=9Hz, 2H), 6.77(s, 2H), 5.11(s, 1H), 5.01(bs, 1H), 4.13(t, J=7Hz, 2H), 3.75-3.95(m, 3H), 2.91-3.03(m, 2H), 2.75-2.90(m, 4H), 1.92-2.03(m, 2H), 1.25-1.40(m, 2H), 1.37(s, 18H)
IR(cm^{-1}) 3314, 2948, 1638, 1602, 1544, 1303, 1226, 1153, 768

Example 101

N-[2-(3,5-di-tert-butyl-4-hydroxystyryl)phenyl]-N'-(2-pyridylmethyl)urea



(1) To a solution of 4-(2-aminostyryl)-2,6-di-tert-butylphenol (4.85 g, 15.0 mmol) and diisopropylamine (1.72 g, 17.0 mmol) in methylene chloride (30 ml) was added dropwise under ice-cooling phenyl chloroformate (2.51 g, 16.0 mmol). The mixture was stirred for 7 hrs, while returning slowly to room temperature. To the mixture was added diisopropylamine (0.51 g, 5.0 mmol) and added dropwise under ice-cooling diisopropylamine (0.51 g, 5.0 mmol).

This mixture was stirred for 3 hrs, while returning slowly to room temperature. The reaction solution was washed with water and a saturated NaCl solution, dried over $MgSO_4$ and concentrated. Purification of the residue by a silica gel column chromatography gave N-[2-(3,5-di-tert-butyl-4-hydroxystyryl)phenyl]phenyl carbamate (6.65 g, 99%) as a viscous oil.

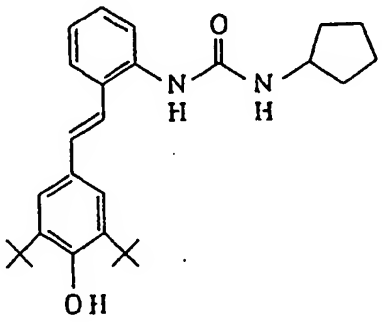
^{1}H-NMR(δ ppm, $CDCl_3$) 7.91(b, 1H), 6.90-7.53(m, 13H), 5.35(s, 1H), 1.49(s, 18H)

(2) A solution of N-[2-(3,5-di-tert-butyl-4-hydroxystyryl)phenyl]phenyl carbamate (1.00 g, 2.25 mmol) and 2-(aminomethyl)pyridine (0.27 g, 2.50 mmol) in xylene (5 ml) was stirred at 80-100°C for 3 hrs. After distilling off the solvent, purification of the residue by a silica gel column chromatography afforded N-[2-(3,5-di-tert-butyl-4-hydroxystyryl)phenyl]-N'-(2-pyridylmethyl)urea (0.54 g, 71%) as crystals. m.p. 207-210°C

^{1}H-NMR(δ ppm, $CDCl_3$) 8.37(d, J=4Hz, 1H), 7.59(dd, J=8, 2Hz, 1H), 7.51(d, J=7Hz, 1H), 7.43-7.50(m, 1H), 7.31(s, 2H), 7.16-7.28(m, 3H), 7.17(d, J=16Hz, 1H), 7.02-7.07(m, 1H), 6.99(d, J=16Hz, 1H), 6.68-6.91(m, 1H), 5.79-5.87(m, 1H), 5.32(s, 1H), 4.51(d, J=5Hz, 2H), 1.45(s, 18H)
IR(cm^{-1}) 3350, 3270, 2960, 1640, 1560, 1475, 1440, 1235, 1010, 755, 740

Example 102

N-[2-(3,5-di-tert-butyl-4-hydroxystyryl)phenyl]-N'-cycloheptylurea

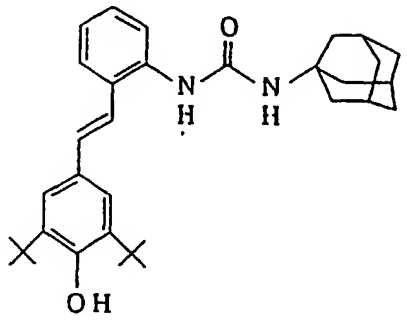


The title compound was prepared in a similar manner to that mentioned in Example 101, using cycloheptylamine instead of 2-(aminomethyl)pyridine.
m.p. 203-206°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.61(d, J=8Hz, 1H), 7.38(d, J=8Hz, 1H), 7.33(s, 2H), 7.18-7.28(m, 2H), 7.06(d, J=16Hz, 1H), 7.00(d, J=16Hz, 1H), 6.05(s, 1H), 5.33(s, 1H), 4.48-4.55(m, 1H), 4.04-4.16(m, 1H), 1.88-2.00(m, 2H), 1.48-1.62(m, 4H), 1.47(s, 18H), 1.22-1.37(m, 2H)
IR(cm^{-1}) 3630, 3310, 2950, 1630, 1560, 1440, 1235, 960, 745

Example 103

N-[2-(3,5-di-tert-butyl-4-hydroxystyryl)phenyl]-N'-adamantylurea

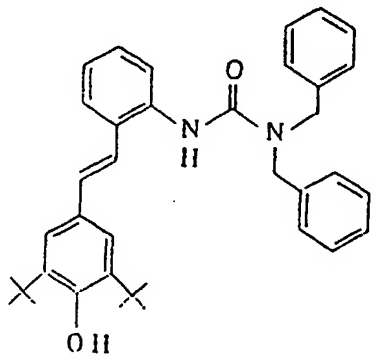


The title compound was prepared in a similar manner to that mentioned in Example 101, using 1-adamantanamine instead of 2-(aminomethyl)pyridine.
m.p. 205-211°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.66(dd, J=7, 2Hz, 1H), 7.34(s, 2H), 7.29-7.36(m, 1H), 7.15-7.29(m, 2H), 7.06(d, J=16Hz, 1H), 7.00(d, J=16Hz, 1H), 5.90(s, 1H), 5.33(s, 1H), 4.34(s, 1H), 1.82-2.06(m, 9H), 1.52-1.67(m, 6H), 1.47(s, 18H)
IR(cm^{-1}) 3630, 3330, 2900, 1640, 1560, 1525, 1235, 740,

Example 104

N-[2-(3,5-di-tert-butyl-4-hydroxystyryl)phenyl]-N',N'-dibenzylurea

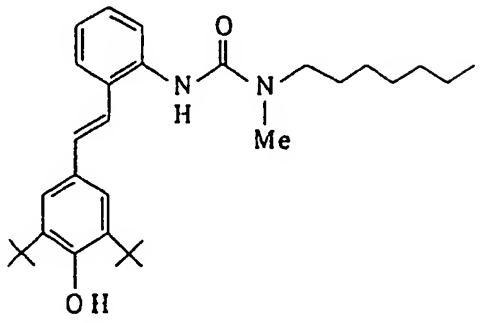


The title compound was prepared in a similar manner to that mentioned in Example 101, using N,N-dibenzylamine instead of 2-(aminomethyl)pyridine.
m.p. 175-178°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.79(dd, J=8, 1Hz, 1H), 7.36(dd, J=8, 1Hz, 1H), 7.02-7.30(m, 13H), 7.02-7.08(m, 1H), 6.78(d, J=16Hz, 1H), 6.65(d, J=16Hz, 1H), 5.31(s, 1H), 4.60(s, 4H), 1.47(s, 18H)
IR(cm^{-1}) 3420, 3390, 2940, 1660, 1580, 1520, 1450, 1435, 1230, 960, 755

Example 105

N-[2-(3,5-di-tert-butyl-4-hydroxystyryl)phenyl]-N'-methyl-N'-heptylurea

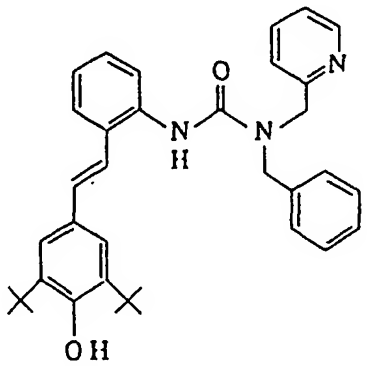


The title compound was prepared in a similar manner to that mentioned in Example 101, using N-methylheptylamine instead of 2-(aminomethyl)pyridine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.81(d, J=8Hz, 1H), 7.44(d, J=8Hz, 1H), 7.32(s, 2H), 7.22-7.27(m, 1H), 7.05-7.10(m, 1H), 7.00(d, J=16Hz, 1H), 6.93(d, J=16Hz, 1H), 6.36(s, 1H), 5.32(s, 1H), 3.34(d, J=8Hz, 2H), 3.02(s, 3H), 1.54-1.65(m, 2H), 1.47(s, 18H), 1.16-1.32(m, 8H), 0.84(t, J=7Hz, 3H)
IR(cm^{-1}) 3640, 3450, 3300, 2960, 2930, 1640, 1580, 1520, 1485, 1440, 1240, 1155, 960, 750

Example 106

N-[2-(3,5-di-tert-butyl-4-hydroxystyryl)phenyl]-N'-benzyl-N'-(2-pyridylmethyl)urea

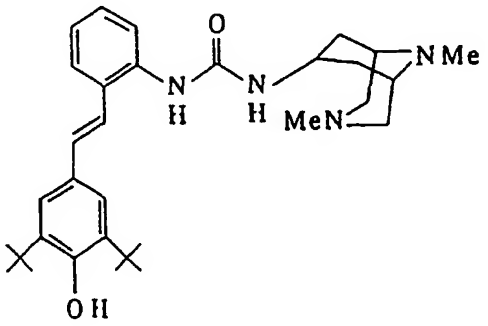


The title compound was prepared in a similar manner to that mentioned in Example 101, using 2-(benzylaminomethyl)pyridine instead of 2-(aminomethyl)pyridine.

^{1}H-NMR(δ ppm, $CDCl_3$) 9.74(b, 1H), 8.14(d, J=4Hz, 1H), 7.87(d, J=8Hz, 1H), 7.47-7.57(m, 1H), 7.18-7.34(m, 9H), 6.88-7.11(m, 4H), 5.26(s, 1H), 4.65(s, 2H), 4.49(s, 2H), 1.40(s, 18H)
IR(cm^{-1}) 3390, 2950, 1660, 1580, 1525, 1455, 1230, 960, 755, 735, 700

Example 107

N-[2-(3,5-di-tert-butyl-4-hydroxystyryl)phenyl]-N'-(3,9-dimethyl-3,9-diazabicyclo[3-3.1]-7-nonyl)urea

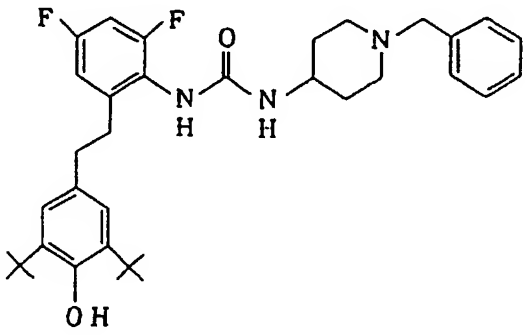


The title compound was prepared in a similar manner to that mentioned in Example 101, using 7-amino-3,9-dimethyl-3,9-diazabicyclo[3.3.1]nonane instead of 2-(aminomethyl)pyridine.
m.p. 188-191°C

^{1}H-NMR(δ ppm, $CDCl_3$) 8.78(d, J=10Hz, 1H), 7.64(dd, J=7, 2Hz, 1H), 7.30-7.35(m, 3H), 7.13-7.27(m, 2H), 7.13(d, J=2Hz, 1H), 7.02(d, J=2Hz, 1H), 5.93(s, 1H), 5.35(s, 1H), 4.22-4.33(m, 1H), 2.66-2.72(m, 2H), 2.41(s, 3H), 2.22-2.40(m, 6H), 1.48(s, 3H), 1.47(s, 18H), 1.28-1.38(m, 2H)
IR(cm^{-1}) 3410, 2940, 1630, 1600, 1510, 1440, 1390, 1265, 1185, 965, 760

Example 108

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]-N'-(1-benzyl-4-piperidyl)urea



(1) To a solution of 4-(2-amino-3,5-difluorophenethyl)-2,6-di-tert-butylphenol (1.37 g, 3.8 mmol) and diisopropylamine (0.50 g, 4.9 mmol) in methylene chloride (20 ml) was added dropwise under ice-cooling phenyl chloroformate (0.66 g, 4.2 mmol) and the mixture was stirred for 3 hrs, while returning slowly to room temperature. Diisopropylamine (0.19 g, 1.9 mmol) was further added and phenyl chloroformate (0.30 g, 1.9 mmol) was added dropwise under ice-cooling. The mixture was stirred for 3 hrs while returning slowly to room temperature. The reaction solution was washed with water and a saturated NaCl solution, dried over $MgSO_4$ and concentrated. Purification of the residue by silica gel column chromatography gave N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]phenyl carbamate (1.82 g, 99%) as oil.

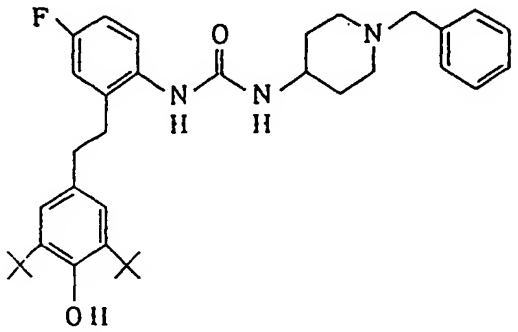
^{1}H-NMR(δ ppm, $CDCl_3$) 7.04-7.42(m, 5H), 6.67-6.85(m, 4H), 5.16(s, 1H), 4.94(s, 1H), 2.76-3.02(m, 4H), 1.37(s, 18H)

(2) A solution of N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]phenyl carbamate (1.82 g, 3.8 mmol) and 4-amino-1-benzylpyridine (0.72 g, 3.8 mmol) in toluene (10 ml) was stirred at 100-120°C for 2 hrs. After distilling off the solvent, purification of the residue by a silica gel column chromatography afforded N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]-N'-(1-benzyl-4-piperidyl)urea (1.39 g, 64%) as a noncrystalline solid.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.20-7.30(m, 5H), 6.65-6.80(m, 4H), 5.12(s, 1H), 4.79(bs, 1H), 4.14(bd, J=8Hz, 1H), 3.54-3.66(m, 1H), 3.44(s, 2H), 2.84(d, J=7Hz, 2H), 2.70-2.79(m, 4H), 1.98-2.10(m, 2H), 1.80-1.92(m, 2H), 1.30-1.40(m, 20H)
IR(cm^{-1}) 3638, 3316, 2952, 1639, 1562, 1494, 1436, 1235, 1122

Example 109

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4-fluorophenyl]-N'-(1-benzyl-4-piperidyl)urea

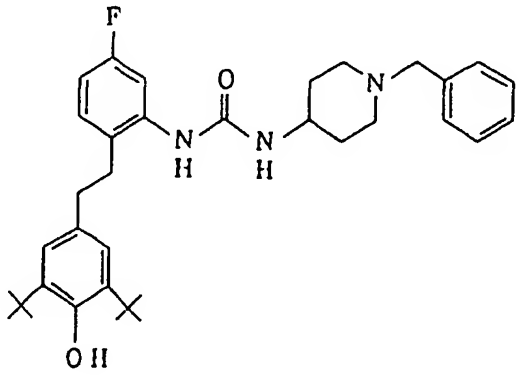


The title compound was prepared in a similar manner to that mentioned in Example 108, using 4-(2-amino-5-fluorophenethyl)-2,6-di-tert-butylphenol instead of 4-(2-amino-3,5-difluorophenethyl)-2,6-di-tert-butylphenol.
m.p. 108-109°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.21-7.31(m, 5H), 7.16(dd, J=9, 5Hz, 1H), 6.87-6.96(m, 2H), 6.77(s, 2H), 5.12(s, 1H), 4.86(s, 1H), 3.99(d, J=8Hz, 1H), 3.55-3.70(m, 1H), 3.44(s, 1H), 2.70-2.85(m, 6H), 2.05(t, J=11Hz, 2H), 1.85(d, J=10Hz, 2H), 1.38(s, 18H), 1.25-1.35(m, 2H)
IR(cm^{-1}) 3636, 3280, 1634, 1561, 1495, 1435, 1234, 1213, 1120, 739, 699

Example 110

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-5-fluorophenyl]-N'-(1-benzyl-4-piperidyl)urea

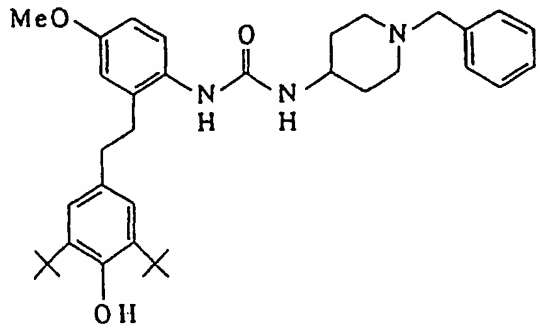


The title compound was prepared in a similar manner to that mentioned in Example 108, using 4-(2-amino-4-fluorophenethyl)-2,6-di-tert-butylphenol instead of 4-(2-amino-3,5-difluorophenethyl)-2,6-di-tert-butylphenol.
m.p. 118-119°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.20-7.32(m, 5H), 7.13-7.20(m, 2H), 6.84(dt, J=3, 8Hz, 1H), 6.78(s, 2H), 5.13(s, 1H), 5.01(s, 1H), 4.02(d, J=8Hz, 1H), 3.46-3.63(m, 1H), 3.46(s, 2H), 2.77(bs, 6H), 2.06(t, J=11Hz, 2H), 1.86(d, J=11Hz, 2H), 1.38(s, 18H), 1.30-1.40(m, 2H)
IR(cm^{-1}) 3630, 3350, 1640, 1602, 1563, 1434, 1233, 738, 700

Example 111

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4-methoxyphenyl]-N'-(1-benzyl-4-piperidyl)urea

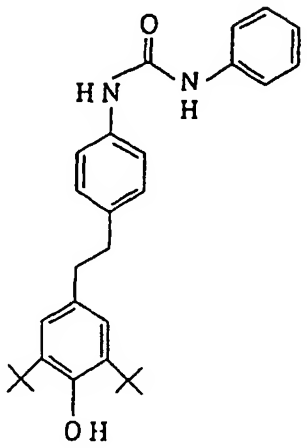


The title compound was prepared in a similar manner to that mentioned in Example 108, using 4-(2-amino-5-methoxyphenethyl)-2,6-di-tert-butylphenol instead of 4-(2-amino-3,5-difluorophenethyl)-2,6-di-tert-butylphenol.
m.p. 174-175°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.20-7.30(m, 5H), 7.00-7.07(m, 1H), 6.78(s, 2H), 6.70-6.75(m, 2H), 5.09(s, 1H), 4.91(s, 1H), 4.05(d, J=8Hz, 1H), 3.79(s, 3H), 3.60-3.65(m, 1H), 3.43(s, 2H), 2.70-2.80(m, 6H), 2.05(t, J=11Hz, 2H), 1.85(d, J=11Hz, 2H), 1.38(s, 18H), 1.20-1.40(m, 2H)
IR(cm^{-1}) 3630, 3312, 1634, 1561, 1501, 1436, 1282, 1231, 1055, 880, 750, 710

Example 112

N-[4-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-phenylurea

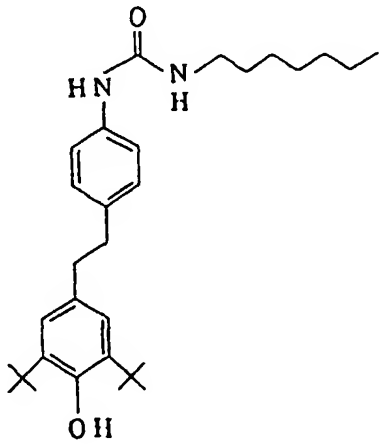


The title compound was prepared in a similar manner to that mentioned in Example 1, using 4-(4-aminophenethyl)-2,6-di-tert-butylphenol instead of 4-(2-aminophenethyl)-2,6-di-tert-butylphenol and using benzoic acid instead of 4-hexyloxybenzoic acid. m.p. 206-207°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.22-7.38(m, 6H), 7.18(d, J=9Hz, 2H), 7.08-7.14(m, 1H), 6.55(bs, 1H), 6.47(bs, 1H), 2.77-2.92(m, 4H), 1.43(s, 18H)
IR(cm^{-1}) 3640, 3330, 2960, 1655, 1605, 1565, 1440, 1320, 1240, 760, 695

Example 113

N-[4-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-heptylurea

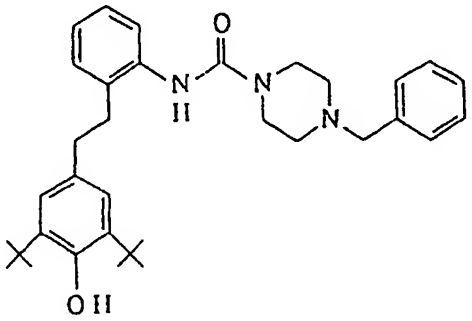


The title compound was prepared in a similar manner to that mentioned in Example 1, using 4-(4-aminophenethyl)-2,6-di-tert-butylphenol instead of 4-(2-aminophenethyl)-2,6-di-tert-butylphenol and n-octanoic acid instead of 4-hexyloxybenzoic acid. m.p. 151-152°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.13-7.21(m, 4H), 6.95(s, 2H), 6.22(bs, 1H), 5.06(s, 1H), 4.73(bt, J=5Hz, 1H), 3.23(dt, J=5, 7Hz, 2H), 2.75-2.90(m, 42H), 1.45-1.54(m, 2H), 1.42(s, 18H), 1.21-1.36(m, 8H), 0.88(t, J=7Hz, 3H)
IR(cm^{-1}) 3630, 3120, 2960, 2930, 2860, 1645, 1605, 1575, 1520, 1440, 1235

Example 114

1-Benzyl-4-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]piperazine

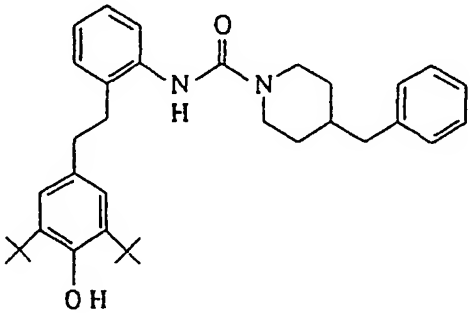


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-benzylpiperazine instead of decylamine. m.p. 70-72°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.49-7.51(m, 1H), 7.09-7.33(m, 8H), 6.78(s, 2H), 5.61(s, 1H), 5.06(s, 1H), 3.50(s, 2H), 3.22(t, J=5Hz, 4H), 2.80(s, 4H), 2.39(t, J=5Hz, 4H), 1.33(s, 18H)
IR(cm^{-1}) 3636, 3310, 2952, 1635, 1516, 1435, 1234, 1001, 754

Example 115

4-Benzyl-1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]piperidine

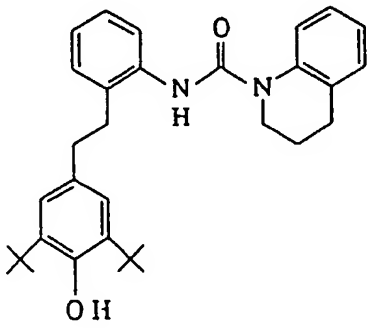


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-benzylpiperidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.52(d, J=8Hz, 1H), 7.06-7.32(m, 8H), 6.79(s, 2H), 5.67(s, 1H), 5.06(s, 1H), 3.68-3.76(m, 2H), 2.81(s, 4H), 2.62-2.72(m, 2H), 2.53(t, J=7Hz, 4H), 1.50-1.73(m, 3H), 1.35(s, 18H), 1.10-1.23(m, 2H)
IR(cm^{-1}) 3645, 3440, 3330, 2960, 2925, 1645, 1525, 1455, 1440, 1250, 755, 705

Example 116

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-1,2,3,4-tetrahydroquinoline

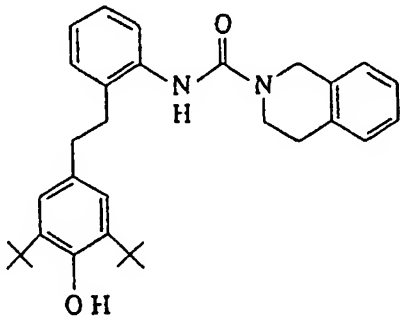


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1,2,3,4-tetrahydroquinoline instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.82(d, J=7Hz, 1H), 7.36(d, J=7Hz, 1H), 7.13-7.21(m, 2H), 7.16(d, J=7Hz, 1H), 6.99-7.09(m, 3H), 6.89(bs, 1H), 6.82(s, 2H), 5.06(s, 1H), 3.80(t, J=6Hz, 2H), 2.78(t, J=6Hz, 2H), 2.69(s, 4H), 1.98(m, 2H), 1.39(s, 18H)
IR(cm^{-1}) 3630, 3434, 2946, 1671, 1524, 1492, 1435, 1304, 1236, 753

Example 117

2-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-1,2,3,4-tetrahydroisoquinoline

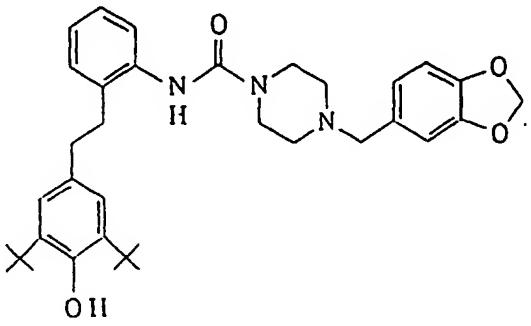


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1,2,3,4-tetrahydroisoquinoline instead of decylamine. m.p. 148-150°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.55(d, J=8Hz, 1H), 7.10-7.26(m, 7H), 6.83(s, 1H), 5.73(bs, 1H), 5.10(s, 1H), 4.52(s, 2H), 3.44(t, J=6Hz, 2H), 2.86(t, J=6Hz, 2H), 2.84(s, 4H), 1.36(s, 18H)
IR(cm^{-1}) 3628, 3312, 1630, 1515, 1459, 1437, 1373, 1231, 747

Example 118

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-4-(3,4-methylenedioxybenzyl)piperazine

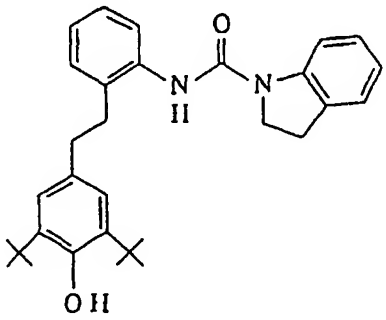


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-(3,4-methylenedioxybenzyl)piperazine instead of decylamine.
m.p. 149-151°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.50(d, J=7Hz, 1H), 7.18-7.23(m, 2H), 7.11(dd, J=7, 7Hz, 1H), 6.83(s, 1H), 6.70-6.76(m, 2H), 5.95(s, 2H), 5.61(bs, 1H), 5.06(s, 1H), 3.40(s, 2H), 3.22(t, J=5Hz, 4H), 2.80(s, 4H), 2.36(t, J=5Hz, 4H), 1.34(s, 18H)
IR(cm^{-1}) 3626, 3302, 2956, 1632, 1504, 1491, 1438, 1247, 1040, 999, 759

Example 119

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]indoline

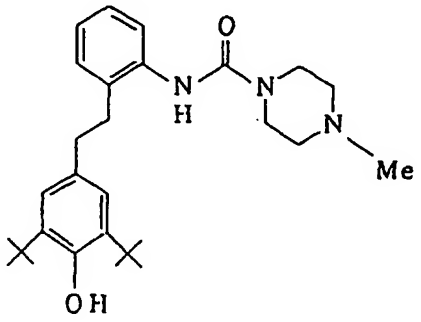


The title compound was prepared in a similar manner to that mentioned in Example 11, using indoline instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.91(d, J=8Hz, 1H), 7.61(d, J=8Hz, 1H), 7.10-7.30(m, 2H), 6.91(dd, J=8, 8Hz, 2H), 6.81(d, J=8Hz, 2H), 6.78(s, 2H), 5.65(bs, 1H), 5.10(s, 1H), 3.57(t, J=8Hz, 2H), 3.14(t, J=8Hz, 2H), 2.86(s, 4H), 1.35(s, 18H)
IR(cm^{-1}) 3622, 3272, 2952, 1654, 1594, 1507, 1485, 1448, 1347, 1234, 753

Example 120

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-4-methylpiperazine

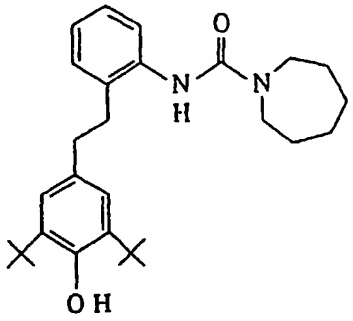


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-methylpiperazine instead of decylamine. m.p. 134-137°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.47(d, J=8Hz, 1H), 7.17-7.26(m, 2H), 7.12(ddd, J=7, 7, 2Hz, 1H), 6.79(s, 2H), 5.56(s, 1H), 5.10(s, 1H), 3.25(t, J=5Hz, 4H), 2.82(s, 4H), 2.35(t, J=5Hz, 4H), 2.29(s, 3H), 1.37(s, 18H)
IR(cm^{-1}) 3632, 3440, 2940, 1636, 1511, 1437, 1002, 750

Example 121

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]perhydroazepine

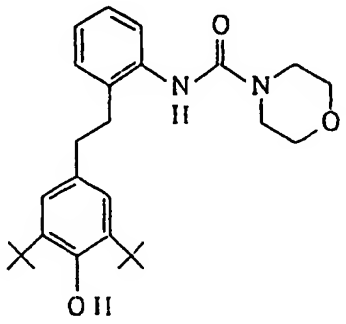


The title compound was prepared in a similar manner to that mentioned in Example 11, using hexamethyleneimine instead of decylamine. m.p. 136-138°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.67(dd, J=7, 2Hz, 1H), 7.17-7.24(m, 2H), 7.08(ddd, J=7, 7, 2Hz, 1H), 6.82(s, 2H), 5.78(s, 1H), 5.08(s, 1H), 3.26-3.34(m, 4H), 2.82(bs, 1H), 1.66-1.74(m, 4H), 1.52-1.59(m, 4H), 1.37(s, 18H)
IR(cm^{-1}) 3460, 1660, 1587, 1525, 1453, 1436, 755

Example 122

4-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]morpholine

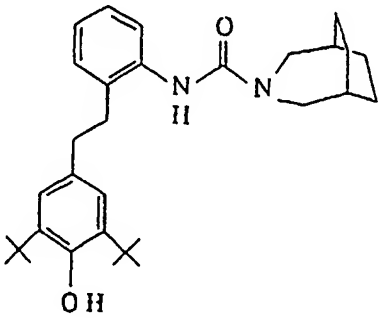


The title compound was prepared in a similar manner to that mentioned in Example 11, using morpholine instead of decylamine. m.p. 186-189°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.47(dd, J=8, 2Hz, 1H), 7.19-7.27(m, 2H), 7.14(ddd, J=7, 7, 2Hz, 1H), 6.78(s, 2H), 5.52(s, 1H), 5.09(s, 1H), 3.64(t, J=5Hz, 4H), 3.19(t, J=5Hz, 4H), 2.82(s, 4H), 1.36(s, 18H)
IR(cm^{-1}) 3644, 3420, 3290, 2956, 1631, 1525, 1435, 1262, 1118, 756

Example 123

3-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-3-azabicyclo[3.2.2]nonane

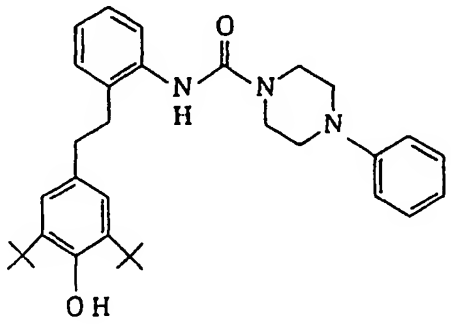


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3-azabicyclo[3.2.2]nonane instead of decylamine.
m.p. 184-186°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.52(d, J=8Hz, 1H), 7.26-7.34(m, 2H), 7.09(dd, J=7, 7Hz, 1H), 6.81(s, 2H), 5.71(s, 1H), 5.08(s, 1H), 3.40(d, J=4Hz, 4H), 2.82(s, 4H), 1.96-2.04(m, 2H), 1.57-1.72(m, 8H), 1.37(s, 18H)
IR(cm^{-1}) 3630, 3430, 3334, 2930, 2860, 1627, 1511, 754

Example 124

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-4-phenylpiperazine

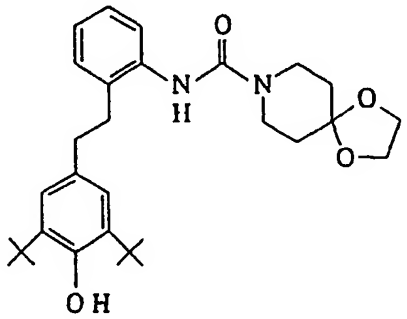


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-phenylpiperazine instead of decylamine. m.p. 155-156°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.11-7.48(m, 6H), 6.88-6.92(m, 1H), 6.89(d, J=8Hz, 2H), 6.79(s, 2H), 5.61(t, J=5Hz, 4H), 3.12(t, J=5Hz, 4H), 2.83(s, 4H), 1.37(s, 18H)
IR(cm^{-1}) 3584, 3372, 2960, 1639, 1601, 1505, 1435, 1234, 999, 753

Example 125

8-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-1,4-dioxa-8-azaspiro[4.5]decane

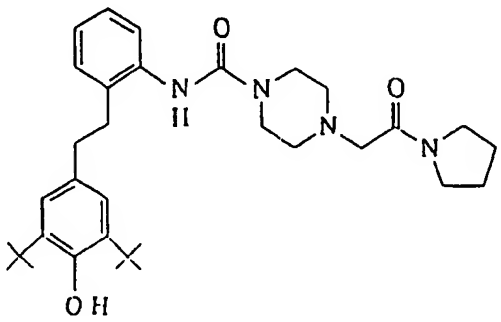


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1,4-dioxa-8-azaspiro[4.5]decane instead of decylamine. m.p. 163-164°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.45(d, J=7Hz, 1H), 7.17-7.26(m, 2H), 7.12(dd, J=7, 7Hz, 1H), 6.78(s, 2H), 5.59(bs, 1H), 5.09(s, 1H), 3.96(s, 4H), 3.30(t, J=6Hz, 4H), 2.82(s, 4H), 1.65(t, J=6Hz, 4H), 1.36(s, 18H)
IR(cm^{-1}) 3430, 3300, 2955, 1645, 1510, 1490, 1455, 1440, 1250, 1120, 950, 750

Example 126

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-4-(1-pyrrolidinylcarbonylmethyl)piperazine

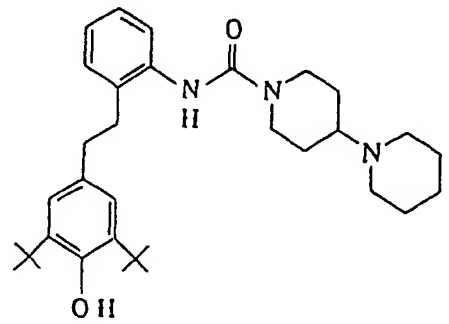


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-(1-pyrrolidinylcarbonylmethyl)piperazine instead of decylamine.
m.p. 212-214°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.47(d, J=8Hz, 1H), 7.16-7.25(m, 2H), 7.11(ddd, J=7, 7, 1Hz, 1H), 6.78(s, 2H), 5.59(s, 1H), 5.10(s, 1H), 3.45-3.52(m, 4H), 3.28(t, J=5Hz, 4H), 3.11(s, 2H), 2.81(s, 4H), 2.50(t, J=5Hz, 4H), 1.80-2.00(m, 4H), 1.36(s, 18H)
IR(cm^{-1}) 3500, 3328, 2960, 1626, 1521, 1457, 1437, 750

Example 127

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-4-piperidinopiperidine

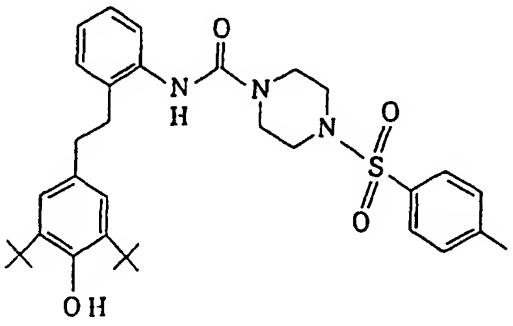


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-piperidinopiperidine instead of decylamine. m.p. 64-67°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.48(d, J=7Hz, 1H), 7.16-7.25(m, 2H), 7.11(ddd, J=7, 7, 2Hz, 1H), 6.79(s, 2H), 5.62(s, 1H), 5.09(s, 1H), 3.73-3.81(m, 2H), 2.81(s, 4H), 2.65-2.75(m, 2H), 2.44-2.51(m, 4H), 2.33-2.44(m, 1H), 1.75-1.82(m, 2H), 1.54-1.62(m, 4H), 1.39-1.50(m, 4H), 1.37(s, 18H)
IR(cm^{-1}) 3636, 3420, 2934, 1640, 1520, 1450, 1250, 750

Example 128

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-4-(p-toluenesulfonyl)piperazine

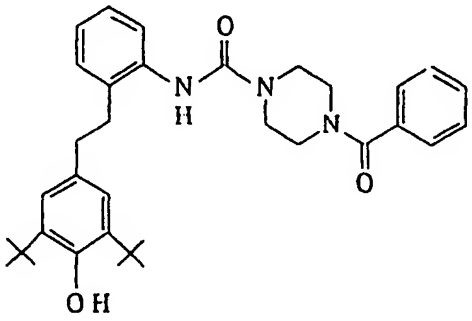


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-(p-toluenesulfonyl)piperazine instead of decylamine.
m.p. 195-197°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.61(d, J=8Hz, 2H), 7.29-7.36(m, 3H), 7.19-7.24(m, 3H), 6.73(s, 2H), 5.41(bs, 1H), 5.12(s, 1H), 3.26(t, J=5Hz, 4H), 2.93(t, J=5Hz, 4H), 2.70-2.83(m, 4H), 2.45(s, 3H), 1.35(s, 18H)
IR(cm^{-1}) 3630, 3410, 2950, 1635, 1625, 1350, 1170, 730

Example 129

1-Benzoyl-4-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]piperazine

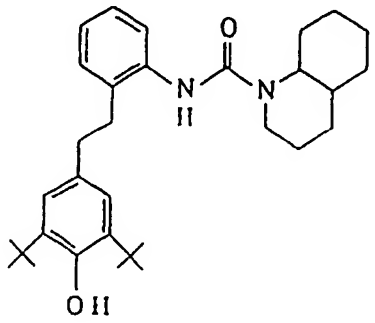


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-benzoylpiperazine instead of decylamine. m.p. 207-209°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.37-7.48(m, 6H), 7.12-7.27(m, 3H), 6.76(s, 2H), 5.52(bs, 1H), 5.08(s, 1H), 3.12-3.85(m, 8H), 2.82(s, 4H), 1.33(s, 18H)
IR(cm^{-1}) 3570, 3266, 2950, 1629, 1530, 1435, 1260, 1007, 754

Example 130

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]decahydroquinoline

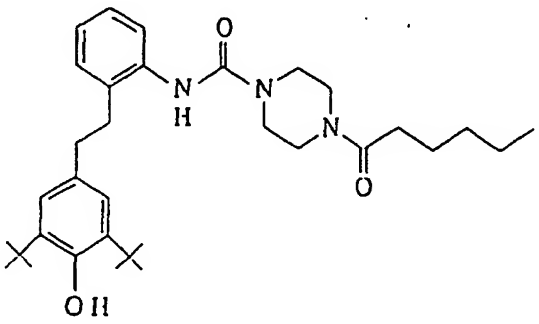


The title compound was prepared in a similar manner to that mentioned in Example 11, using decahydroquinoline instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.57(d, J=8Hz, 1H), 7.12-7.21(m, 2H), 7.07(dd, J=7, 7Hz, 1H), 6.86(s, 2H), 5.88(bs, 1H), 5.08(s, 1H), 4.06(m, 1H), 3.45(m, 1H), 2.75-2.90(m, 5H), 1.90(m, 1H), 1.63-1.80(m, 4H), 1.20-1.60(m, 8H), 1.39(m, 18H)
IR(cm^{-1}) 3430, 2924, 1632, 1510, 1434, 750

Example 131

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-4-pentanoylpiperazine

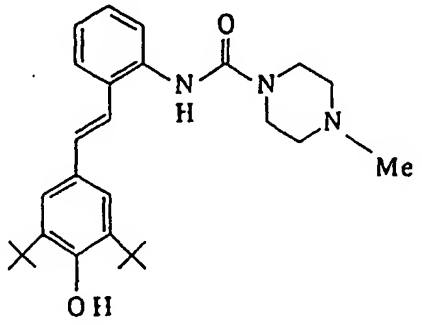


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-pentanoylpiperazine instead of decylamine. m.p. 126-128°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.44(d, J=9Hz, 1H), 7.12-7.27(m, 3H), 6.77(s, 2H), 5.52(bs, 1H), 5.12(s, 1H), 3.56-3.63(m, 2H), 3.40-3.46(m, 2H), 3.27-3.34(m, 2H), 3.08-3.14(m, 2H), 2.82(s, 4H), 2.30(t, J=5Hz, 2H), 1.58-1.67(m, 2H), 1.36(s, 18H), 1.28-1.38(m, 4H)
IR(cm^{-1}) 3300, 2952, 1636, 1530, 1435, 1240, 994, 755

Example 132

1-[N-[2-(3,5-di-tert-butyl-4-hydroxystyryl)phenyl]carbamoyl]-4-methylpiperazine

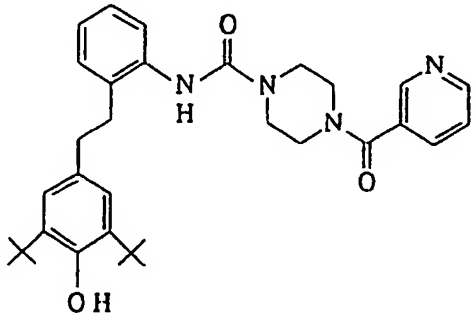


The title compound was prepared in a similar manner to that mentioned in Example 101, using 1-methylpiperazine instead of 2-(aminomethyl)pyridine. m.p. 192-194°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.65(d, J=8Hz, 1H), 7.46-7.50(m, 1H), 7.33(s, 2H), 7.20-7.26(m, 1H), 7.11(dd, J=9, 1Hz, 1H), 6.99(d, J=16Hz, 1H), 6.94(d, J=16Hz, 1H), 6.39(bs, 1H), 5.34(s, 1H), 3.51(t, J=5Hz, 4H), 2.43(t, J=5Hz, 4H), 2.32(m, 3H), 1.47(s, 18H)
IR(cm^{-1}) 3636, 3420, 3288, 2952, 1635, 1525, 1485, 1439, 1236, 1149, 959, 765, 755

Example 133

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-4-nicotinoylpiperazine

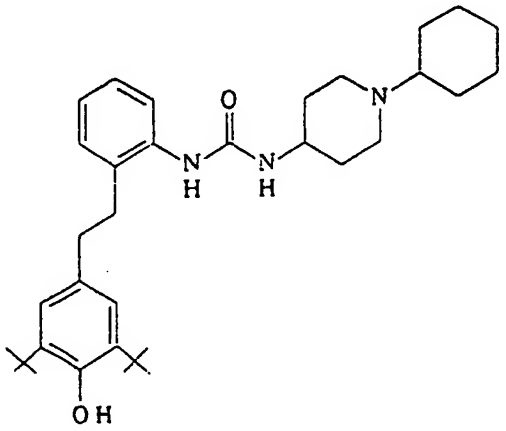


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-nicotinoylpiperazine instead of decylamine. m.p. 171-172°C

^{1}H-NMR(δ ppm, $CDCl_3$) 8.70(dd, J=5, 2Hz, 1H), 8.66(d, J=1Hz, 1H), 7.75(ddd, J=8, 8, 2Hz, 1H), 7.36-7.42(m, 2H), 7.14-7.27(m, 3H), 6.75(s, 2H), 5.52(s, 1H), 5.11(s, 1H), 3.10-3.80(m, 8H), 2.82(s, 4H), 1.33(s, 18)
IR(cm^{-1}) 3636, 3420, 3288, 2952, 1635, 1525, 1485, 1439, 1236, 1149, 959, 765, 755

Example 134

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-cyclohexyl-4-piperidyl)urea

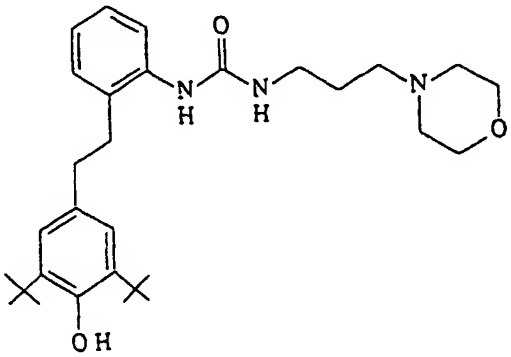


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-cyclohexylpiperidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.15-7.25(m, 4H), 6.79(s, 2H), 5.38(bs, 2H), 5.12(s, 1H), 4.55(bs, 1H), 3.65-3.75(m, 1H), 2.90-2.98(m, 2H), 2.75-2.90(m, 4H), 2.35-2.45(m, 3H), 1.85-2.00(m, 4H), 1.78(bs, 2H), 1.45-1.65(m, 3H), 1.38(s, 18H), 1.00-1.35(m, 5H)
IR(cm^{-1}) 3638, 3262, 1658, 1643, 1560, 1542, 1435, 1233, 754

Example 135

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(3-morpholinopropyl)urea

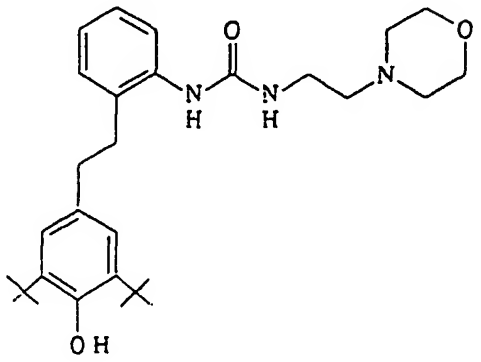


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-(3-aminopropyl)morpholine instead of decylamine. m.p. 138-139°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.19-7.29(m, 4H), 6.80(s, 2H), 5.19(bs, 1H), 5.12(s, 1H), 5.04(t, J=5Hz, 1H), 3.44(bs, 4H), 3.25(q, J=6Hz, 2H), 2.77-2.87(m, 4H), 2.25-2.35(m, 6H), 1.60(quint., J=7Hz, 2H), 1.38(s, 18H)
IR(cm^{-1}) 3528, 3304, 1633, 1565, 1436, 1238, 1116, 872, 752

Example 136

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(2-morpholinoethyl)urea

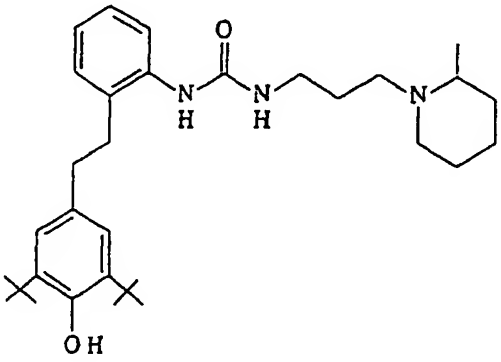


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-(2-aminoethyl)morpholine instead of decylamine. m.p. 166-167°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.19-7.28(m, 4H), 6.80(s, 2H), 5.19(s, 1H), 5.14(s, 1H), 4.91(s, 1H), 3.56(t, J=6Hz, 4H), 3.24(t, J=6Hz, 2H), 2.75-2.89(m, 4H), 2.30-2.42(m, 6H), 1.38(s, 18H)
IR(cm^{-1}) 3566, 3326, 1643, 1574, 1436, 1300, 1238, 1116, 755

Example 137

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[3-(2-methyl-1-piperidyl)propyl]urea

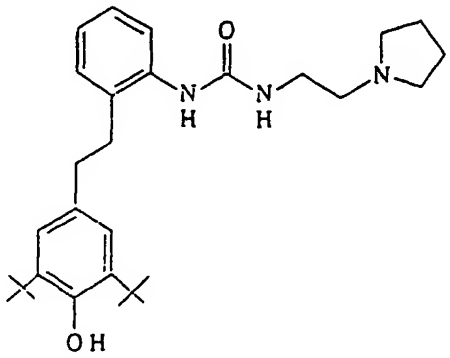


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-(3-aminopropyl)-2-methylpiperidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.14-7.30(m, 4H), 6.81(s, 2H), 5.43(bs, 1H), 5.36(bs, 1H), 5.11(s, 1H), 3.15-3.30(m, 2H), 2.70-2.87(m, 6H), 2.20-2.30(m, 2H), 2.01(t, J=10Hz, 1H), 1.40-1.65(m, 5H), 1.38(s, 18H), 1.00-1.40(m, 3H), 0.98(d, J=6Hz, 3H)
IR(cm^{-1}) 3638, 3294, 1643, 1543, 1436, 1234, 754

Example 138

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[2-(1-pyrrolidinyl)ethyl]urea

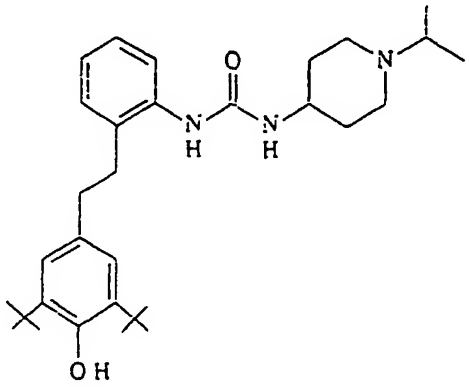


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-(2-aminoethyl)pyrrolidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.37(d, J=7Hz, 1H), 7.11-7.21(m, 3H), 6.82(s, 2H), 5.55(bs, 1H), 5.26(s, 1H), 5.03(s, 1H), 3.29(t, J=6Hz, 2H), 2.65-2.85(m, 5H), 2.59(t, J=6Hz, 2H), 2.53(bs, 3H), 1.74(bs, 4H), 1.38(s, 18H)
IR(cm^{-1}) 3638, 3350, 1686, 1546, 1436, 1234, 753

Example 139

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(2-propyl)-4-piperidyl]urea

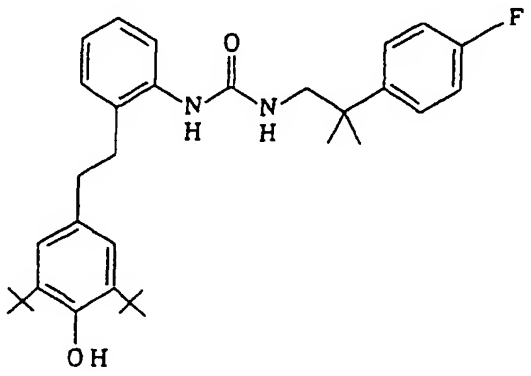


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-(2-propyl)piperidine instead of decylamine. m.p. 191-193°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.15-7.26(m, 4H), 6.78(s, 2H), 5.11(bs, 2H), 4.30(bs, 1H), 3.59-3.72(m, 1H), 2.73-2.90(m, 7H), 2.25-2.37(m, 2H), 1.87-1.98(m, 2H), 1.30-1.50(m, 2H), 1.38(s, 18H), 1.07(d, J=6Hz, 6H)
IR(cm^{-1}) 3358, 2948, 1641, 1561, 1435, 1235

Example 140

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[2-(4-fluorophenyl)-2-methylpropyl]urea

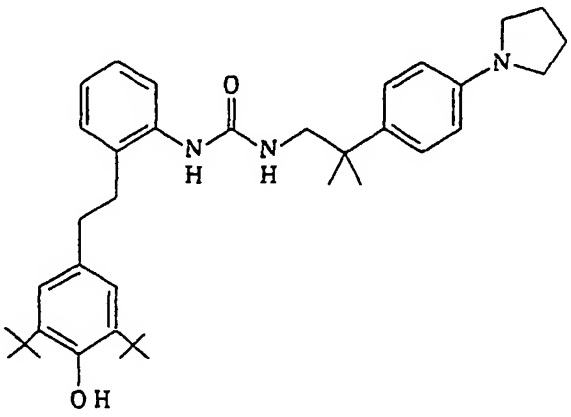


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-fluoro-β,β-dimethylphenethylamine instead of decylamine. m.p. 179-180°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.14-7.20(m, 4H), 7.08(t, J=7Hz, 1H), 6.87-6.96(m, 3H), 6.74(s, 2H), 5.08(s, 1H), 5.00(s, 1H), 3.95-4.05(m, 1H), 3.30(d, J=6Hz, 2H), 2.70-2.80(m, 4H), 1.36(s, 18H), 1.24(s, 6H)
IR(cm^{-1}) 3638, 3370, 1644, 1653, 1613, 1436, 1231, 1166, 833, 762

Example 141

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[2-[4-(1-pyrrolidinyl)phenyl]-2-methylpropyl]urea

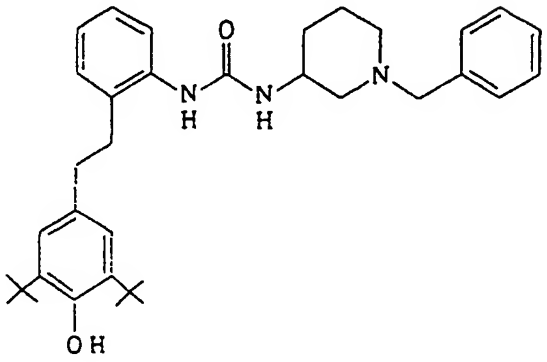


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-[4-(1-amino-2-methyl-2-propyl)phenyl]pyrrolidine instead of decylamine.
m.p. 195-196°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.02-7.18(m, 6H), 6.77(s, 2H), 6.43(d, J=9Hz, 2H), 5.08(s, 2H), 4.14(t, J=6Hz, 1H), 3.28(t, J=6Hz, 2H), 3.22-3.25(m, 4H), 2.70-2.78(m, 4H), 1.97-2.01(m, 4H), 1.37(s, 18H), 1.23(s, 6H)
IR(cm^{-1}) 3642, 3354, 1642, 1615, 1562, 1524, 1369, 1234, 814, 750

Example 142

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-benzyl-3-piperidyl)urea

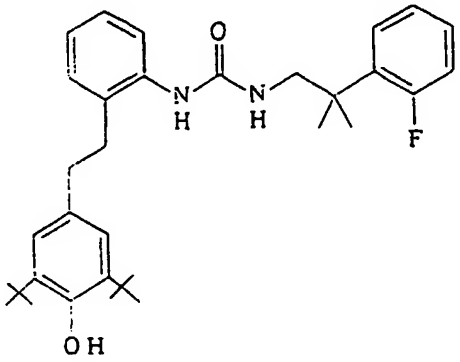


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3-amino-1-benzylpiperidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.20-7.40(m, 9H), 6.79(s, 2H), 5.12(bs, 1H), 5.09(s, 1H), 3.87-3.96(m, 1H), 3.49(bs, 1H), 3.37(d, J=13Hz, 1H), 3.28(d, J=13Hz, 1H), 2.70-2.90(m, 4H), 2.40-2.50(m, 2H), 1.30-1.70(m, 24H)
IR(cm^{-1}) 3632, 3338, 2948, 1639, 1542, 1435, 1234, 744, 699

Example 143

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[2-(2-fluorophenyl)-2-methylpropyl]urea

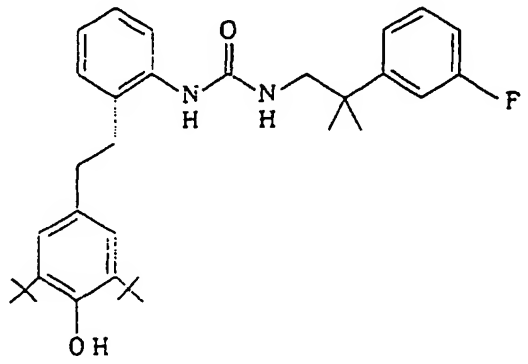


The title compound was prepared in a similar manner to that mentioned in Example 11, using 2-fluoro-β,β-dimethylphenethylamine instead of decylamine. m.p. 182-183°C

^{1}H-NMR(δ ppm, $CDCl_3$) 6.88-7.21(m, 8H), 6.75(s, 2H), 5.07(s, 1H), 5.02(s, 1H), 4.02-4.09(m, 1H), 3.50(d, J=6Hz, 2H), 2.67-2.78(m, 4H), 1.36(s, 18H), 1.33(s, 6H)
IR(cm^{-1}) 3650, 3330, 2960, 1640, 1575, 1445, 1255, 765

Example 144

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[2-(3-fluorophenyl)-2-methylpropyl]urea

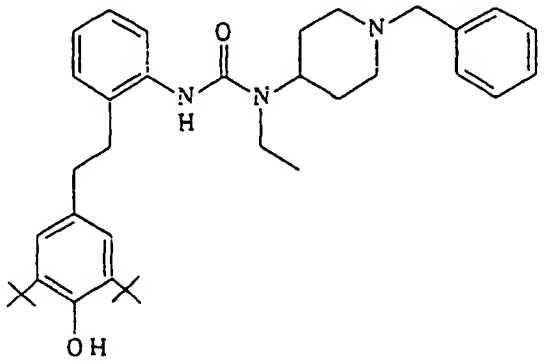


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3-fluoro-β,β-dimethylphenethylamine instead of decylamine. m.p. 165-166°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.04-7.23(m, 4H), 6.80-7.00(m, 4H), 6.74(s, 2H), 5.08(s, 1H), 4.94(s, 1H), 3.98(t, J=6Hz, 1H), 3.32(d, J=6Hz, 2H), 2.68-2.79(m, 4H), 1.36(s, 18H), 1.25(s, 6H)
IR(cm^{-1}) 3640, 3350, 2970, 1645, 1615, 1590, 1560, 1440, 910, 765, 700

Example 145

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-benzyl-4-piperidyl)-N'-ethylurea

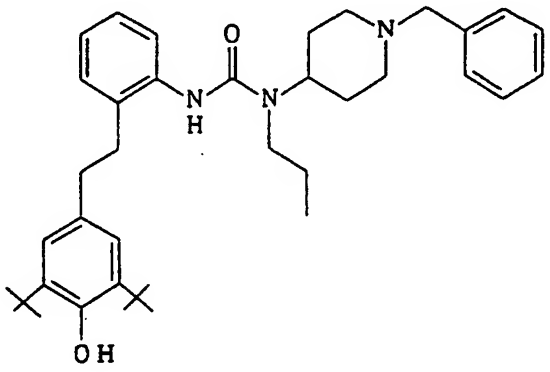


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-ethylamino-1-benzylpiperidine instead of decylamine. m.p. 149-151°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.72(d, J=8Hz, 1H), 7.15-7.33(m, 7H), 7.07(t, J=7Hz, 1H), 6.83(s, 2H), 5.91(bs, 1H), 5.07(s, 1H), 4.16-4.38(m, 1H), 3.48(s, 2H), 3.02(q, J=7Hz, 2H), 2.93(d, J=12Hz, 2H), 2.82(bs, 4H), 2.03-2.10(m, 2H), 1.60-1.75(m, 4H), 1.37(s, 18H), 1.16(t, J=7Hz, 3H)
IR(cm^{-1}) 3334, 2954, 1631, 1520, 1502, 1263, 1202, 743

Example 146

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-benzyl-4-piperidyl)-N'-propylurea

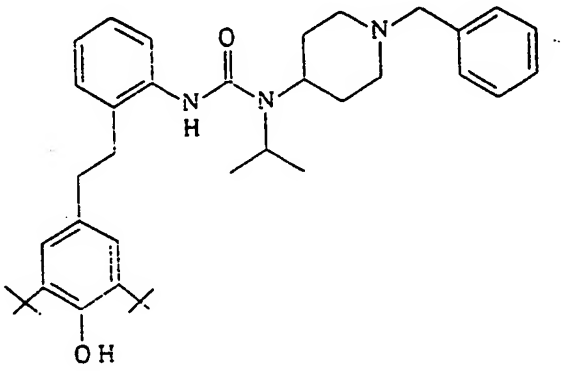


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-benzyl-4-propylaminopiperidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.76(d, J=7Hz, 1H), 7.10-7.35(m, 7H), 7.04(td, J=6, 1Hz, 1H), 6.87(s, 2H), 6.07(bs, 1H), 5.06(s, 1H), 4.12-4.23(m, 1H), 3.48(s, 2H), 3.04(bt, J=8Hz, 2H), 2.94(d, J=12Hz, 2H), 2.81(s, 4H), 2.00-2.10(m, 2H), 1.50-1.75(m, 6H), 1.39(s, 18H), 0.86(t, J=7Hz, 3H)
IR(cm^{-1}) 3634, 3450, 2956, 1650, 1509, 1451, 1234, 742

Example 147

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-benzyl-4-piperidyl)-N'-(2-propyl)urea

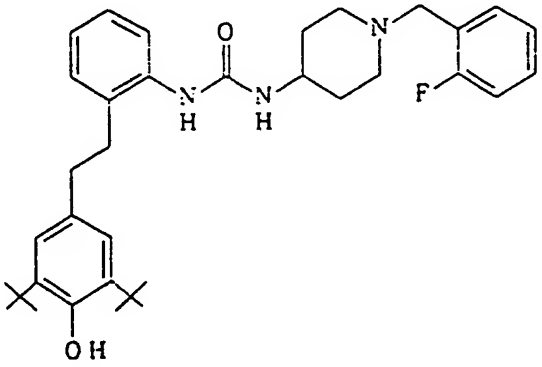


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-benzyl-4-[(2-propyl)amino]piperidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.65(d, J=8Hz, 1H), 7.10-7.30(m, 7H), 7.04(td, J=7, 1Hz, 1H), 6.89(s, 2H), 6.03(bs, 1H), 5.05(s, 1H), 3.70-3.90(m, 2H), 3.47(s, 2H), 2.75-2.98(m, 6H), 1.90-2.05(m, 4H), 1.55-1.70(m, 2H), 1.39(s, 18H), 1.31(d, J=7Hz, 6H)
IR(cm^{-1}) 3450, 2954, 1650, 1521, 1451, 1237, 744

Example 148

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(2-fluorobenzyl)-4-piperidyl]urea



The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-(2-fluorobenzyl)piperidine instead of decylamine.

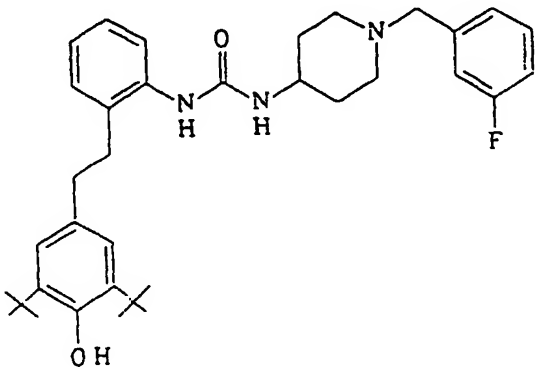
m.p. 136-137°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.14-7.34(m, 6H), 6.95-7.10(m, 2H), 6.77(s, 2H), 5.10(s, 1H), 4.99(s, 1H), 4.10(d, J=8Hz, 1H), 3.55-3.71(m, 1H), 3.52(s, 2H), 2.68-2.88(m, 6H), 2.07-2.17(m, 2H), 1.82-1.90(m, 2H), 1.37(s, 18H), 1.24-1.35(m, 2H)

IR(cm^{-1}) 3640, 3340, 2960, 1650, 1590, 1570, 1495, 1235, 765

Example 149

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(3-fluorobenzyl)-4-piperidyl]urea



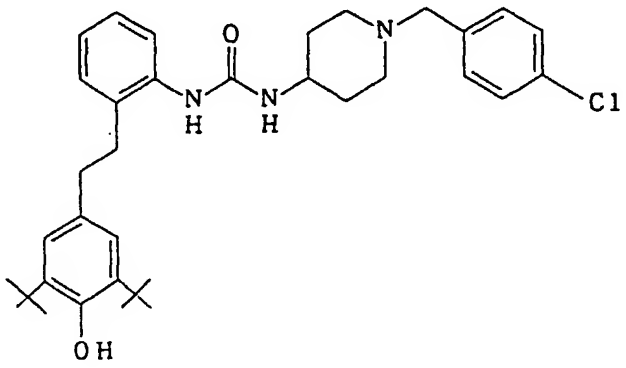
The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-(3-fluorobenzyl)piperidine instead of decylamine. m.p. 99-100°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.15-7.27(m, 5H), 7.67-7.04(m, 2H), 6.86-6.94(m, 1H), 5.10(s, 1H), 4.12(d, J=8Hz, 1H), 3.57-3.70(m, 1H), 3.42(s, 2H), 2.66-2.86(m, 6H), 2.06(t, J=12Hz, 2H), 1.86(d, J=12Hz, 2H), 1.38(s, 18H), 1.24-

1.35(m, 2H)
IR(cm^{-1}) 3635, 3340, 2950, 1640, 1590, 1565, 1490, 1440, 1235, 880, 750, 690

Example 150

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(4-chlorobenzyl)-4-piperidyl]urea

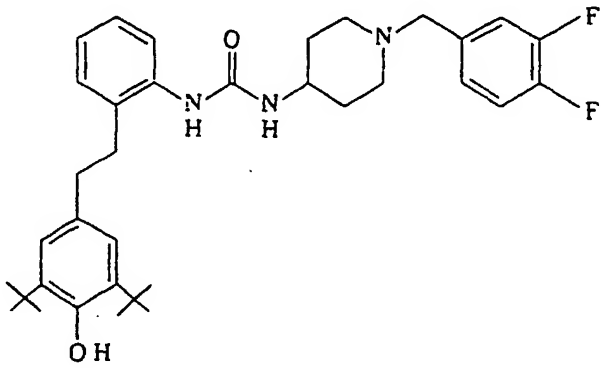


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-(4-chlorobenzyl)piperidine instead of decylamine.
m.p. 184-185°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.15-7.32(m, 8H), 6.77(s, 2H), 5.10(s, 1H), 4.98(s, 1H), 4.09(d, J=8Hz, 1H), 3.57-3.70(m, 1H), 3.39(s, 2H), 2.74-2.87(m, 4H), 2.69(d, J=11Hz, 2H), 2.04(t, J=11Hz, 2H), 1.81-1.88(m, 2H), 1.37(s, 18H), 1.14-1.22(m, 2H)
IR(cm^{-1}) 3645, 3360, 2940, 1640, 1590, 1555, 1490, 1435, 1295, 1235, 1095, 750

Example 151

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(3,4-difluorobenzyl)-4-piperidyl]urea

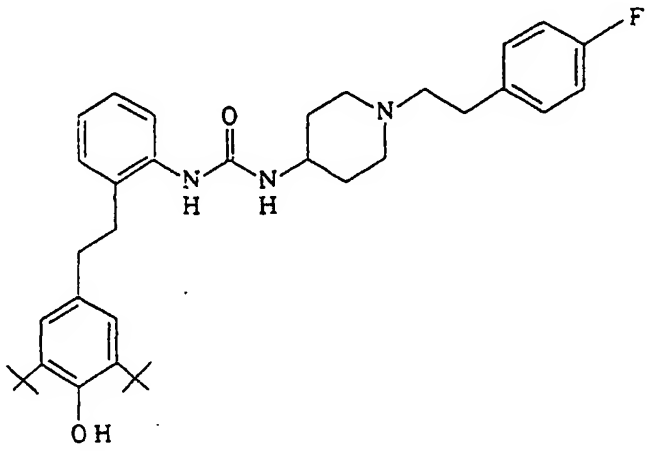


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-(3,4-difluorobenzyl)piperidine instead of decylamine.
m.p. 155-156°C

^{1}H-NMR(δ ppm, $CDCl_3$) 6.92-7.28(m, 7H), 6.77(s, 2H), 5.10(s, 1H), 4.97(s, 1H), 4.08(d, J=8Hz, 1H), 3.58-3.72(m, 1H), 3.37(s, 2H), 2.74-2.87(m, 4H), 2.05(t, J=11Hz, 2H), 1.82-1.90(m, 2H), 1.38(s, 18H), 1.24-1.35(m, 2H)
IR(cm^{-1}) 3650, 3370, 2965, 1645, 1570, 1525, 1440, 1295, 1240, 885, 785, 765

Example 152

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl)-N'-[1-(4-fluorophenethyl)-4-piperidyl]urea

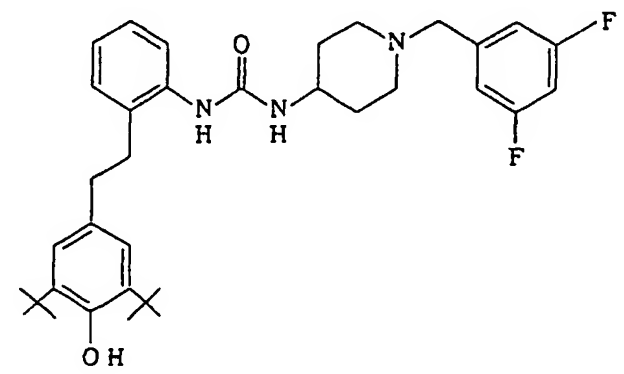


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-(4-fluorophenethyl)piperidine instead of decylamine.
m.p. 117-119°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.10-7.20(m, 6H), 6.94(td, J=7, 2Hz, 2H), 6.78(s, 2H), 5.11(s, 1H), 5.04(bs, 1H), 4.13(bd, J=8Hz, 1H), 3.58-3.70(m, 1H), 2.70-2.90(m, 8H), 2.45-2.55(m, 2H), 2.08-2.12(m, 2H), 1.85-1.95(m, 2H), 1.30-1.40(m, 2H), 1.38(s, 18H)
IR(cm^{-1}) 3630, 3314, 2948, 1634, 1565, 1510, 1228, 748

Example 153

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(3,5-difluorobenzyl)-4-piperidyl]urea

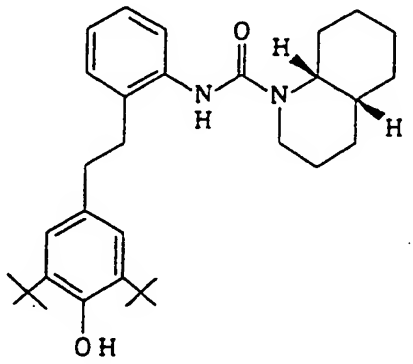


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-amino-1-(3,5-difluorobenzyl)piperidine instead of decylamine.
m.p. 119-120°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.17-7.28(m, 4H), 6.82(d, J=6Hz, 2H), 6.77(s, 2H), 6.62-6.69(m, 1H), 5.11(s, 1H), 4.97(s, 1H), 4.09(d, J=8Hz, 1H), 3.58-3.71(m, 1H), 3.40(s, 2H), 2.66-2.88(m, 6H), 2.07(t, J=11Hz, 2H), 1.83-1.92(m, 2H), 1.38(s, 18H), 1.25-1.36(m, 2H)
IR(cm^{-1}) 3640, 3350, 2960, 1635, 1605, 1505, 1440, 1325, 1235, 1120, 995, 855

Example 154

2-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-cis-decahydroquinoline

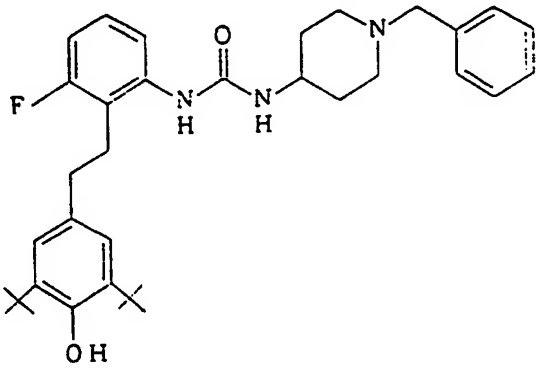


The title compound was prepared in a similar manner to that mentioned in Example 11, using cis-decahydroquinoline instead of decylamine. m.p. 132-133°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.64(d, J=8Hz, 1H), 7.23-7.30(m, 2H), 7.11(t, J=7Hz, 1H), 6.93(s, 2H), 5.94(s, 1H), 5.14(s, 1H), 4.09-4.20(m, 1H), 3.48-3.59(m, 1H), 2.83-2.94(m, 5H), 1.50-2.00(m, 9H), 1.45(s, 18H), 1.24-1.42(m, 4H)
IR(cm^{-1}) 3640, 3320, 2925, 2860, 1630, 1515, 1435, 1360, 1275, 1235, 1160, 755

Example 155

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-3-fluorophenyl]-N'-(1-benzyl-4-piperidyl)urea

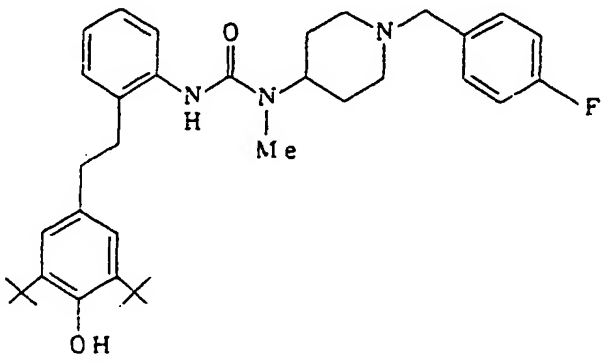


The title compound was prepared in a similar manner to that mentioned in Example 108, using 4-(2-amino-6-fluorophenethyl)-2,6-di-tert-butylphenol instead of 4-(2-amino-3,5-difluorophenethyl)-2,6-di-tert-butylphenol.
m.p. 103-105°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.20-7.35(m, 5H), 7.13(t, J=8Hz, 1H), 7.03(d, J=8Hz, 1H), 6.93(t, J=9Hz, 1H), 6.75(s, 2H), 5.13(s, 1H), 4.60(bs, 1H), 3.95(bd, J=8Hz, 1H), 3.54-3.66(m, 1H), 3.44(s, 2H), 2.70-2.90(m, 6H), 2.00-2.10(m, 2H), 1.80-1.90(m, 2H), 1.30-1.40(m, 2H), 1.36(s, 18H)
IR(cm^{-1}) 3630, 3300, 2948, 1632, 1565, 1452, 1235, 699

Example 156

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[1-(4-fluorobenzyl)-4-piperidyl]-N'-methylurea

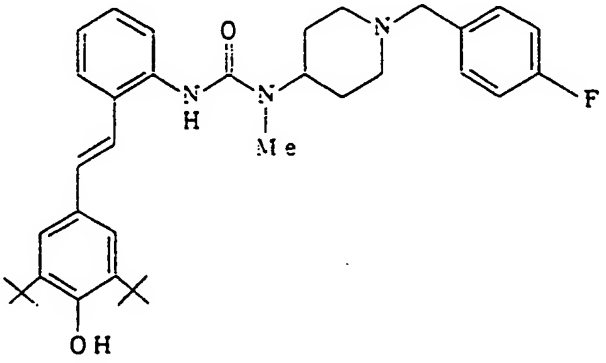


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-(4-fluorobenzyl)-4-(methylamino)piperidine instead of decylamine. m.p. 177-178°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.63(d, J=8Hz, 1H), 7.17-7.28(m, 4H), 7.08-7.13(m, 1H), 6.95-7.03(m, 2H), 6.78(s, 2H), 5.61(s, 1H), 5.08(s, 1H), 4.17-4.28(m, 1H), 3.43(s, 2H), 2.90(d, J=12Hz, 2H), 2.81(s, 4H), 2.50(s, 3H), 1.98-2.07(m, 2H), 1.54-1.68(m, 4H), 1.35(s, 18H)
IR(cm^{-1}) 3630, 3330, 2970, 1635, 1520, 1440, 1330, 1230, 1050, 760,

Example 157

N-[2-(3,5-di-tert-butyl-4-hydroxystyryl)phenyl]-N'-[1-(4-fluorobenzyl)-4-piperidyl]-N'-methylurea

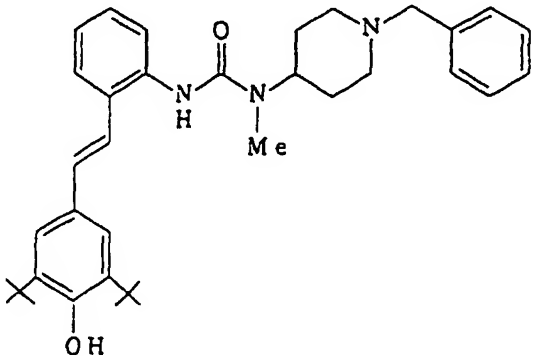


The title compound was prepared in a similar manner to that mentioned in Example 101, using 1-(4-fluorobenzyl)-4-(methylamino)piperidine instead of 2-(aminomethyl)pyridine. m.p. 174-175°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.79(d, J=8Hz, 1H), 7.45(dd, J=7, 1Hz, 1H), 7.31(s, 2H), 7.20-7.30(m, 3H), 7.05-7.13(m, 1H), 6.93-7.03(m, 4H), 6.38(s, 1H), 5.32(s, 1H), 4.14-4.26(m, 1H), 3.46(s, 2H), 2.85-2.96(m, 5H), 1.99-2.10(m, 2H), 1.63-1.82(m, 4H), 1.46(s, 18H)
IR(cm^{-1}) 3640, 3450, 2960, 1640, 1510, 1225, 1160, 1045, 965, 760

Example 158

N-[2-(3,5-di-tert-butyl-4-hydroxystyryl)phenyl]-N'-(1-benzyl-4-piperidyl)-N'-methylurea

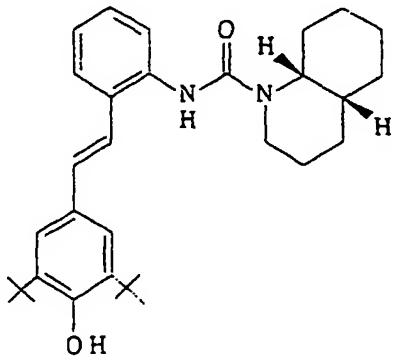


The title compound was prepared in a similar manner to that mentioned in Example 101, using 1-benzyl-4-(methylamino)piperidine instead of 2-(aminomethyl)pyridine.
m.p. 163-164°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.78(d, J=7Hz, 1H), 7.45(dd, J=8, 1Hz, 1H), 7.20-7.35(m, 8H), 7.04-7.12(m, 1H), 7.00(d, J=16Hz, 1H), 6.93(d, J=16Hz, 1H), 6.38(s, 1H), 5.32(s, 1H), 4.14-4.27(m, 1H), 3.48(s, 2H), 2.94(d, J=12Hz, 2H), 2.90(s, 3H), 2.00-2.11(m, 2H), 1.60-1.84(m, 4H), 1.46(s, 18H)
IR(cm^{-1}) 3625, 3440, 3260, 2960, 1635, 1530, 1485, 1240, 1150, 1045, 960, 755, 745, 700

Example 159

2-[N-[2-(3,5-di-tert-butyl-4-hydroxystyryl)phenyl]carbamoyl]-cis-decahydroquinoline

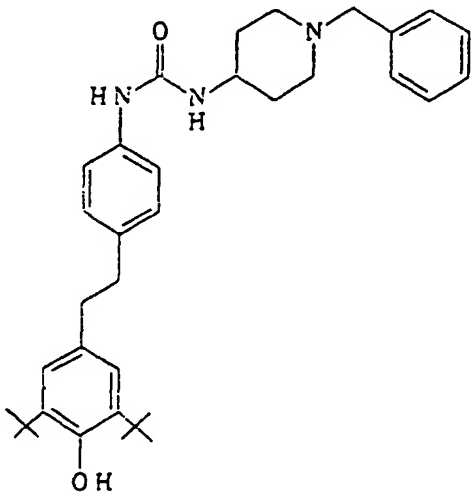


The title compound was prepared in a similar manner to that mentioned in Example 101, using cis-decahydroquinoline instead of 2-(aminomethyl)pyridine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.71(d, J=8Hz, 1H), 7.46(d, J=6Hz, 1H), 7.33(s, 2H), 7.20-7.28(m, 1H), 7.05-7.11(m, 1H), 7.00(d, J=16Hz, 1H), 6.93(d, J=16Hz, 1H), 6.41(s, 1H), 5.32(s, 1H), 3.85-4.07(m, 2H), 1.68-1.97(m, 5H), 1.47-1.64(m, 5H), 1.47(s, 18H), 1.18-1.43(m, 3H)
IR(cm^{-1}) 3640, 3450, 3300, 2930, 2870, 1645, 1525, 1445, 1240, 1160, 965, 755

Example 160

N-[4-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(1-benzyl-4-piperidyl)urea

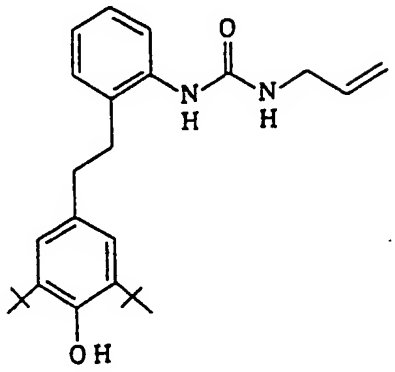


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-(4-aminophenethyl)-2,6-di-tert-butylphenol instead of 4-(2-aminophenethyl)-2,6-di-tert-butylphenol and using 4-amino-1-benzylpiperidine instead of decylamine. m.p. 195-197°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.22-7.34(m, 5H), 7.15(s, 4H), 6.92(s, 2H), 6.10(s, 1H), 5.06(s, 1H), 4.56(d, J=8Hz, 1H), 3.66-3.78(m, 1H), 3.49(s, 2H), 2.75-2.90(m, 6H), 2.07-2.18(m, 2H), 1.91-1.99(m, 2H), 1.36-1.47(m, 2H), 1.43(s, 18H)
IR(cm^{-1}) 3620, 3378, 2946, 1659, 1604, 1542, 1515, 1435, 1324, 1234, 740

Example 161

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-allylurea

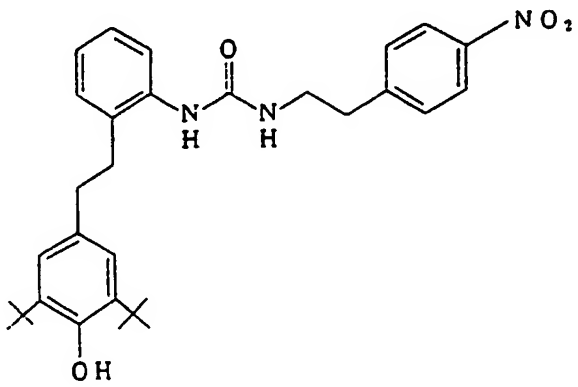


The title compound was prepared in a similar manner to that mentioned in Example 11, using allylamine instead of decylamine. m.p. 169-172°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.16-7.32(m, 5H), 6.78(s, 2H), 5.73-5.85(m, 1H), 4.96-5.14(m, 3H), 4.20-4.26(m, 1H), 3.73-3.80(m, 2H), 2.76-2.90(m, 4H), 1.37(s, 18H)
IR(cm^{-1}) 3632, 3334, 2956, 1653, 1587, 1570, 1561, 1436, 1235, 924, 769

Example 162

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-nitrophenethyl)urea

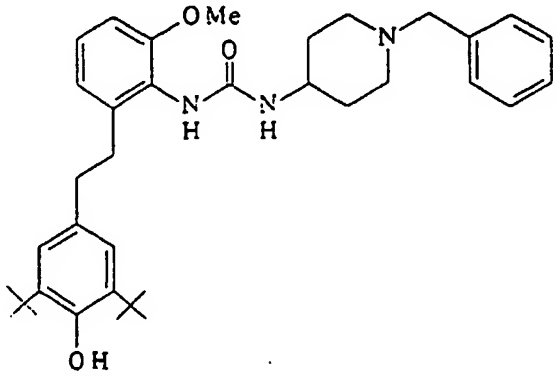


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-nitrophenethylamine instead of decylamine. m.p. 134-136°C

^{1}H-NMR(δ ppm, $CDCl_3$) 8.08(d, J=8Hz, 1H), 7.10-7.29(m, 6H), 6.75(s, 2H), 5.12(s, 1H), 5.05(s, 1H), 4.28(t, J=6Hz, 1H), 3.39(td, J=7, 6Hz, 2H), 2.73-2.90(m, 6H), 1.35(s, 18H)
IR(cm^{-1}) 3630, 3314, 2954, 1639, 1561, 1519, 1436, 1347, 753

Example 163

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-6-methoxyphenyl]-N'-(1-benzyl-4-piperidyl)urea

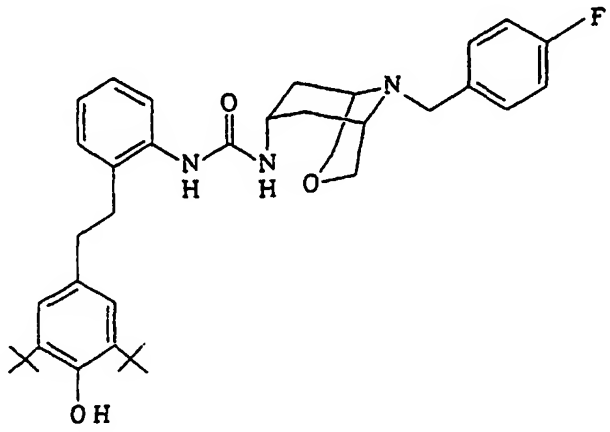


The title compound was prepared in a similar manner to that mentioned in Example 108, using 4-(2-amino-3-methoxyphenethyl)-2,6-di-tert-butylphenol instead of 4-(2-amino-3,5-difluorophenethyl)-2,6-di-tert-butylphenol
m.p. 184-185°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.20-7.30(m, 6H), 6.88(d, J=8Hz, 1H), 6.80(s, 2H), 6.77(d, J=8Hz, 1H), 5.07(s, 1H), 4.88(s, 1H), 4.09(d, J=8Hz, 1H), 3.76(s, 3H), 3.60-3.70(m, 1H), 3.43(s, 2H), 2.86-2.90(m, 2H), 2.70-2.77(m, 4H), 2.05(t, J=11Hz, 2H), 1.86(d, J=10Hz, 2H), 1.38(s, 18H), 1.25(q, J=10Hz, 2H)
IR(cm^{-1}) 3638, 3308, 1653, 1589, 1563, 1556, 1468, 1454, 1435, 1260, 1232, 738

Example 164

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-[endo-9-(4-fluorobenzyl)-3-oxa-9-azabicyclo[3.3.1]non-7-yl]urea

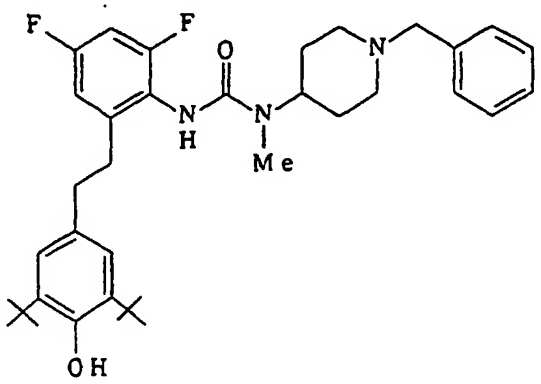


The title compound was prepared in a similar manner to that mentioned in Example 11, using endo-7-amino-9-(4-fluorobenzyl)-3-oxa-9-azabicyclo[3.3.1]nonane instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.18-7.29(m, 6H), 7.06(d, J=11Hz, 1H), 6.99(d, J=9Hz, 1H), 6.96(d, J=9Hz, 1H), 6.83(s, 2H), 5.22(s, 1H), 5.09(s, 1H), 4.37(dd, J=17, 7Hz, 1H), 3.73(d, J=15Hz, 2H), 3.71(s, 2H), 3.39(d, J=11Hz, 2H), 2.84-2.87(m, 2H), 2.76-2.79(m, 2H), 2.52(s, 2H), 2.30-2.37(m, 2H), 1.39(s, 18H), 1.31-1.40(m, 2H)
IR(cm^{-1}) 3636, 3324, 1652, 1525, 1511, 1506, 1436, 1223, 787, 759

Example 165

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]-N'-(1-benzyl-4-piperidyl)-N'-methylurea

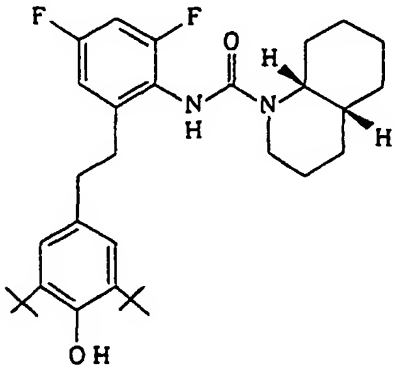


The title compound was prepared in a similar manner to that mentioned in Example 108, using 1-benzyl-4-(methylamino)piperidine instead of 4-amino-1-benzylpiperidine. m.p. 187-191°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.20-7.40(m, 5H), 6.70-6.80(m, 4H), 5.09(s, 1H), 4.91(bs, 1H), 4.10-4.23(m, 1H), 3.47(s, 2H), 2.90-3.00(m, 2H), 2.80-2.90(m, 4H), 2.58(s, 3H), 2.00-2.10(m, 2H), 1.60-1.80(m, 4H), 1.36(s, 18H)
IR(cm^{-1}) 3616, 3312, 1638, 1510, 1436, 1323, 1118

Example 166

2-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]carbamoyl]-cis-decahydroquinoline



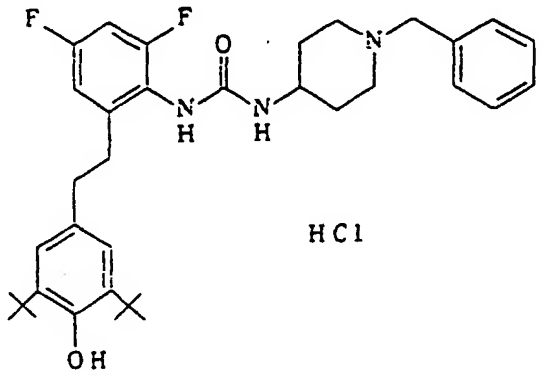
The title compound was prepared in a similar manner to that mentioned in Example 108, using cis-decahydroquinoline instead of 4-amino-1-benzylpiperidine.

m.p. 83-85°C

^{1}H-NMR(δ ppm, $CDCl_3$) 6.83(s, 2H), 6.70-6.80(m, 2H), 5.26(bs, 1H), 5.09(s, 1H), 4.05(bs, 1H), 3.49(bs, 2H), 2.70-2.90(m, 5H), 1.84-1.94(m, 1H), 1.65-1.80(m, 4H), 1.20-1.60(m, 8H), 1.39(s, 18H)
IR(cm^{-1}) 3588, 3316, 2924, 1713, 1638, 1511, 1435, 1120

Example 167

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]-N'-(1-benzyl-4-piperidyl)urea hydrochloride

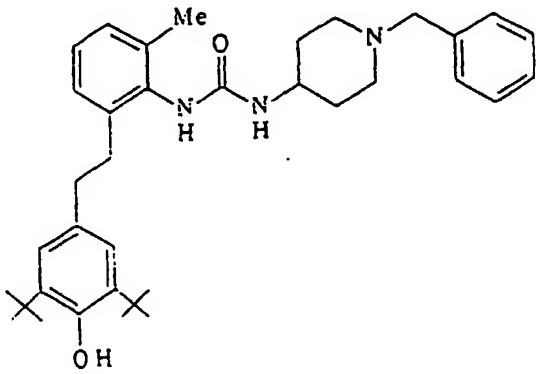


N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]-N'-(1-benzyl-4-piperidyl)urea (1.15 g) was suspended in ethanol (20 ml) and heated at 50°C to dissolve it. To the solution was added 4N hydrochloric acid/ethyl acetate solution (anhydrous)(0.5 ml). This solution was concentrated to a volume of 5 ml, cooled to 0-5°C and allowed to stand for 4 hrs. The resultant crystals were filtered and dried to afford the title compound (1.00 g, 81%).
m.p. 170-175°C

^{1}H-NMR(δ ppm, $CDCl_3$) 12.09(bs, 1H), 7.55(d, J=6Hz, 2H), 7.30-7.40(m, 3H), 6.84(s, 2H), 6.72(d, J=8Hz, 1H), 6.65(td, J=8, 2Hz, 1H), 5.10(s, 1H), 4.12(d, J=7Hz, 1H), 3.75-3.86(m, 1H), 3.35-3.40(m, 2H), 2.65-2.85(m, 6H), 2.10-2.25(m, 4H), 1.39(s, 18H)
IR(cm^{-1}) 3430, 3300, 2952, 1680, 1554, 1436, 1236, 1122

Example 168

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-6-methylphenyl]-N'-(1-benzyl-4-piperidyl)urea

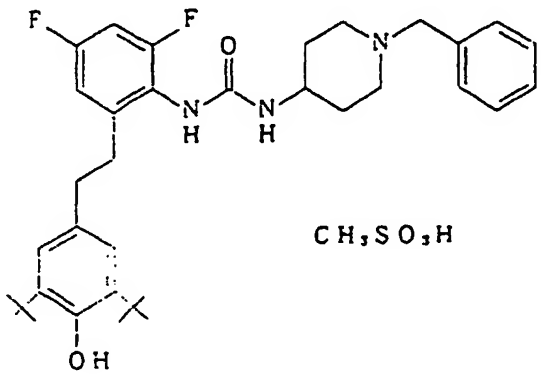


The title compound was prepared in a similar manner to that mentioned in Example 108, using 4-(2-amino-3-methylphenethyl)-2,6-di-tert-butylphenol instead of 4-(2-amino-3,5-difluorophenethyl)-2,6-di-tert-butylphenol.
m.p. 185-186°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.04-7.34(m, 8H), 6.78(s, 2H), 5.08(s, 1H), 4.83(s, 1H), 3.90(d, J=8Hz, 1H), 3.57-3.72(m, 1H), 3.42(s, 2H), 2.62-2.90(m, 6H), 2.19(s, 3H), 2.03(dd, J=12, 11Hz, 2H), 1.83(d, J=11Hz, 2H), 1.38(s, 18H), 1.16-1.32(m, 2H)
IR(cm^{-1}) 3638, 3324, 2950, 1639, 1555, 1436, 1233, 769, 734, 698

Example 169

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]-N'-(1-benzyl-4-piperidyl)urea methanesulfonate



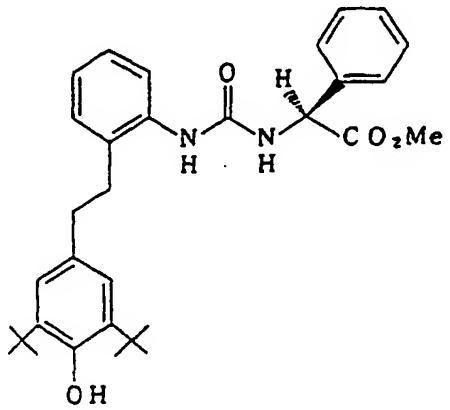
CH_3SO_3H

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]-N'-(1-benzyl-4-piperidyl)urea (0.50 g) was suspended in ethanol (10 ml) and heated at 50°C to dissolve it. To the solution was added methanesulfonic acid (56 µl) and this solution was concentrated. The concentrate was dissolved with a mixed solvent of ethyl acetate (1 ml) and diisopropylether (3 ml). The solution was cooled to 0-5°C and allowed to stand overnight. The resultant crystals were filtered and dried to give the title compound (0.51 g, 87%).
m.p. 252-254°C

^{1}H-NMR(δ ppm, $CDCl_3$) 10.23(bs, 1H), 7.30-7.45(m, 5H), 6.80-6.92(m, 3H), 6.57-6.68(m, 1H), 5.10(s, 1H), 4.30(bs, 1H), 4.12(bs, 1H), 3.74-3.88(m, 1H), 3.40-3.50(m, 2H), 3.20-3.32(m, 1H), 2.60-2.80(m, 9H), 1.90-2.15(m, 4H), 1.39(s, 18H)
IR(cm^{-1}) 3262, 2954, 1657, 1562, 1438, 1220, 1163, 1119, 1041

Example 170

(S)-N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(α-methoxycarbonyl)benzylurea

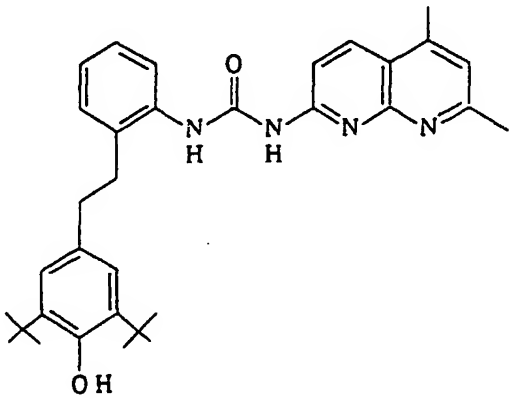


The title compound was prepared in a similar manner to that mentioned in Example 11, using (S)-α-phenylglycine methyl ester instead of decylamine.
m.p. 145-150°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.170-7.34(m, 9H), 6.76(s, 2H), 5.51(d, J=8Hz, 1H), 5.23(d, J=7Hz, 1H), 5.13(s, 1H), 5.09(s, 1H), 3.68(s, 3H), 2.74-2.88(m, 4H), 1.35(s, 18H)
IR(cm^{-1}) 3644, 3345, 2944, 1752, 1644, 1546, 1436, 1211

Example 171

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(2,4-dimethyl-1,8-naphthyridin-7-yl)urea



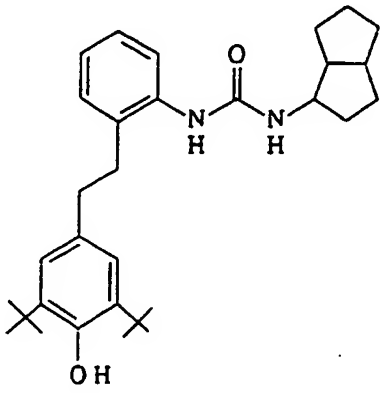
The title compound was prepared in a similar manner to that mentioned in Example 11, using 7-amino-2,4-dimethyl-1,8-naphthyridine instead of decylamine.
m.p. 235-237°C

^{1}H-NMR(δ ppm, $CDCl_3$) 8.22(d, J=9Hz, 1H), 7.86-7.96(m, 1H), 7.10-7.30(m, 3H), 7.02(s, 1H), 6.80(s, 2H), 4.93(s,

1H), 3.15-3.27(m, 2H), 2.90-3.01(m, 2H), 2.62(s, 3H), 2.56(bs, 3H), 1.23(s, 18H)
IR(cm^{-1}) 3636, 2952, 1687, 1615, 1599, 1560, 1527, 1403, 1307, 751

Example 172

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(bicyclo[3.3.0]-2-octyl)urea

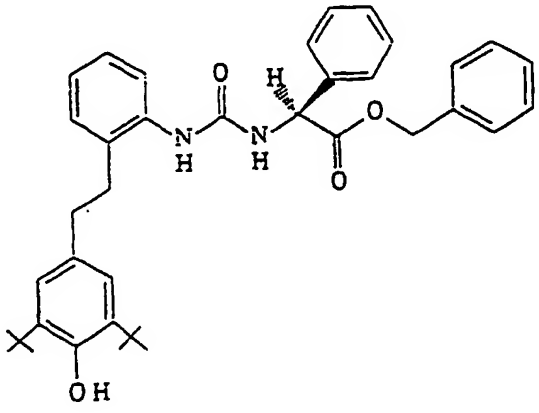


The title compound was prepared in a similar manner to that mentioned in Example 11, using 1-aminobicyclo[3.3.0]octane instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.14-7.29(m, 4H), 6.80(s, 2H), 5.11(s, 1H), 5.060(s, 1H), 4.15(d, J=8Hz, 1H), 3.62-3.72(m, 1H), 2.75-2.88(m, 4H), 2.34-2.45(m, 1H), 1.87-2.01(m, 2H), 1.72-1.83(m, 1H), 1.43-1.63(m, 4H), 1.38(s, 18H), 1.07-1.31(m, 3H)
IR(cm^{-1}) 3634, 2948, 2864, 1637, 1563, 1434, 1231, 760

Example 173

(S)-N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(α-benzyloxycarbonyl)benzylurea



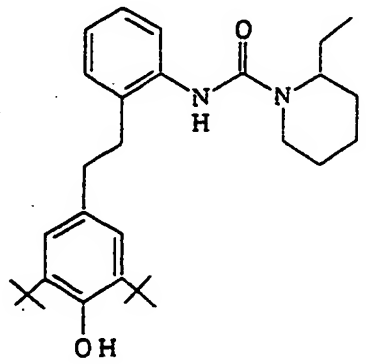
The title compound was prepared in a similar manner to that mentioned in Example 11, using (S)-α-phenylglycine benzyl ester instead of decylamine.

m.p. 132-134°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.13-7.33(m, 14H), 6.75(s, 2H), 5.57(d, J=8Hz, 1H), 5.27(d, J=7Hz, 1H), 5.15(s, 1H), 5.11(s, 2H), 5.08(s, 1H), 2.74-2.87(m, 4H), 1.34(s, 18H)
IR(cm^{-1}) 3642, 3344, 2944, 1749, 1643, 1587, 1553, 1168, 749, 697

Example 174

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-2-ethylpiperidine

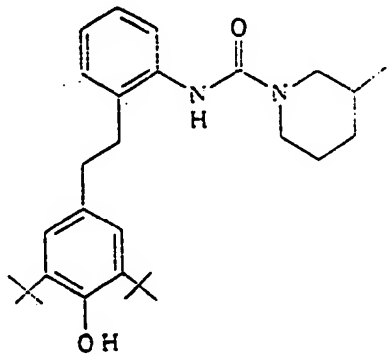


The title compound was prepared in a similar manner to that mentioned in Example 11, using 2-ethylpiperidine instead of decylamine. m.p. 137-138°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.52-7.58(m, 1H), 7.16-7.23(m, 2H), 7.04-7.10(m, 1H), 6.84(s, 2H), 5.78(s, 1H), 5.08(s, 1H), 3.91-4.00(m, 1H), 3.51-3.61(m, 1H), 2.76-2.87(m, 5H), 1.45-1.80(m, 8H), 1.38(s, 18H), 0.86(t, J=7Hz, 3H)
IR(cm^{-1}) 3450, 3300, 2960, 1640, 1510, 1490, 1455, 1250, 885, 765

Example 175

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-3-methylpiperidine



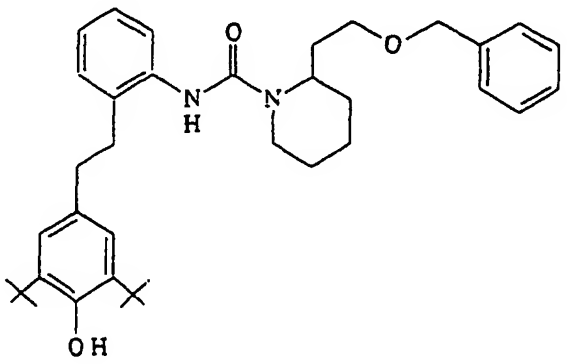
The title compound was prepared in a similar manner to that mentioned in Example 11, using 3-methylpiperidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.49-7.54(m, 1H), 7.16-7.24(m, 2H), 7.07-7.13(m, 1H), 6.83(s, 2H), 5.72(s, 1H), 5.09(s, 1H), 3.80-3.87(m, 1H), 3.46-3.54(m, 1H), 2.82(s, 4H), 2.70-2.82(m, 2H), 2.35-2.44(m, 1H), 1.76-1.84(m, 1H), 1.40-1.67(m, 3H), 1.38(s, 18H), 1.02-1.14(m, 1H), 0.88(t, J=6Hz, 3H)

IR(cm^{-1}) 3645, 3430, 3310, 2960, 2870, 1640, 1525, 1435, 1250, 1150, 750

Example 176

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-2-[2-(benzyloxy)ethyl]piperidine



The title compound was prepared in a similar manner to that mentioned in Example 11, using 2-[2-(benzyloxy)ethyl]methylpiperidine instead of decylamine.

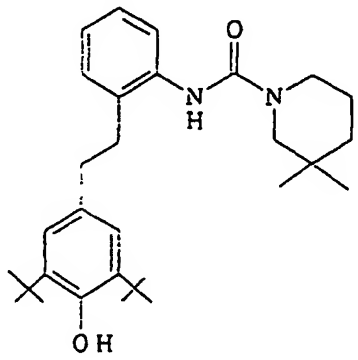
m.p. 113-114°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.53(d, J=8Hz, 1H), 7.02-7.22(m, 8H), 6.89(s, 2H), 6.74(bs, 1H), 5.05(s, 1H), 4.35-4.44(m, 2H), 4.23-4.32(m, 1H), 4.03-4.15(m, 1H), 3.44-3.59(m, 2H), 2.63-2.77(m, 5H), 2.00-2.12(m, 1H), 1.44-1.82(m, 7H), 1.37(s, 18H)

IR(cm^{-1}) 3600, 3420, 2940, 2870, 1665, 1595, 1535, 1450, 1400, 1380, 1270, 1240, 1100, 765, 745

Example 177

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-3,3-dimethylpiperidine



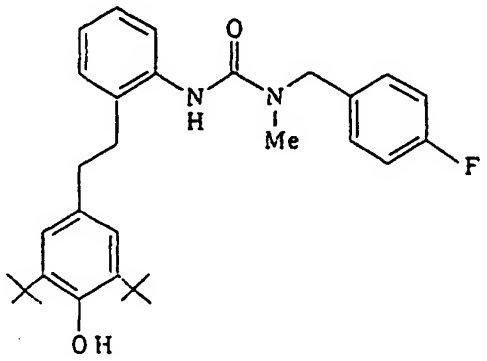
The title compound was prepared in a similar manner to that mentioned in Example 11, using 3,3-dimethylpiperid-

ine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.54(dd, J=8, 1Hz, 1H), 7.16-7.23(m, 2H), 7.04-7.12(m, 1H), 6.84(s, 2H), 5.77(s, 1H), 5.08(s, 1H), 3.19(t, J=6Hz, 2H), 3.05(s, 2H), 2.82(s, 4H), 1.52-1.61(m, 2H), 1.33-1.43(m, 2H), 1.39(s, 18H), 0.92(s, 6H)
IR(cm^{-1}) 3645, 3430, 3320, 2960, 2870, 1640, 1520, 1440, 1250, 1165, 755

Example 178

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(4-fluorobenzyl)-N'-methylurea

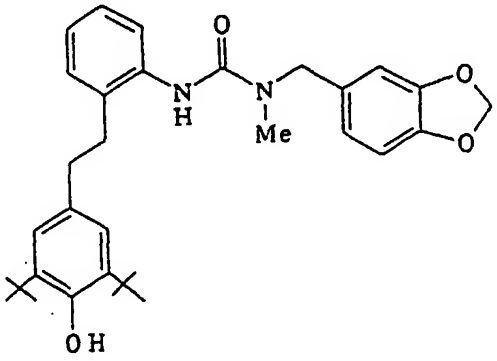


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-fluoro-N-methylphenethylamine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.63(d, J=8Hz, 1H), 7.17-7.26(m, 4H), 7.11(dd, J=8, 7Hz, 1H), 6.97(dd, J=9, 9Hz, 2H), 6.75(s, 2H), 5.66(s, 1H), 5.06(s, 1H), 4.45(s, 2H), 2.73-2.84(m, 4H), 2.64(s, 3H), 1.33(s, 18H)
IR(cm^{-1}) 3645, 3430, 3320, 2965, 1650, 1515, 1440, 1380, 1300, 1230, 1160, 760

Example 179

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]-N'-(3,4-methylenedioxybenzyl)-N'-methylurea

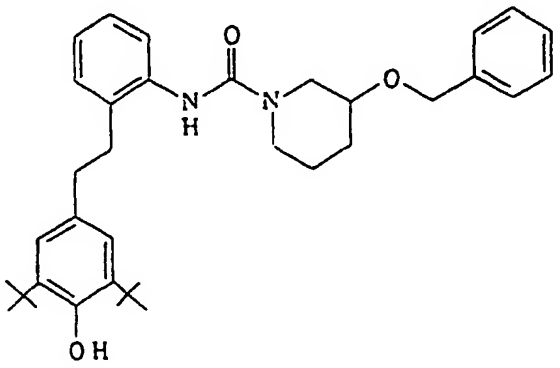


The title compound was prepared in a similar manner to that mentioned in Example 11, using 5-(methylaminomethyl)-1,3-dioxaindane instead of decylamine.
m.p. 152-153°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.65(d, J=8Hz, 1H), 7.16-7.25(m, 2H), 7.10(dd, J=7, 7Hz, 1H), 6.76(s, 2H), 6.65-6.73(m, 2H), 5.92(s, 2H), 5.69(s, 1H), 5.06(s, 1H), 4.39(s, 2H), 2.72-2.83(m, 4H), 2.66(s, 3H), 1.34(s, 18H)

Example 180

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-3-(benzyloxy)piperidine

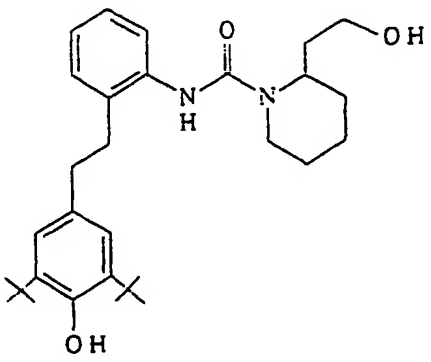


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3-benzyloxypiperidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.44(d, J=8Hz, 1H), 7.22-7.34(m, 5H), 7.18(dd, J=7, 7Hz, 1H), 7.08(dd, J=7, 7Hz, 1H), 6.80(s, 2H), 5.82(s, 1H), 5.06(s, 1H), 4.47-4.56(m, 2H), 3.68-3.76(m, 1H), 3.43-3.51(m, 1H), 3.09-3.22(m, 3H), 2.71-2.83(m, 4H), 1.61-1.96(m, 3H), 1.38-1.50(m, 1H), 1.36(s, 18H)
IR(cm^{-1}) 3625, 3280, 2960, 1635, 1525, 1490, 1445, 1245, 1045, 940, 765

Example 181

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-2-(2-hydroxyethyl)piperidine

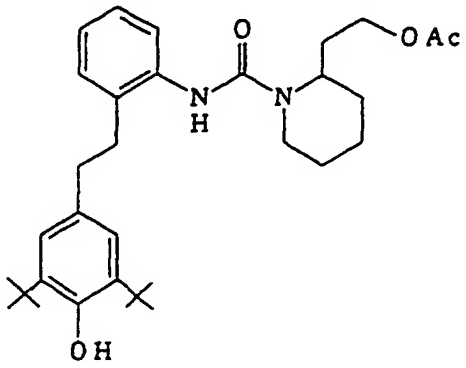


The title compound was prepared in a similar manner to that mentioned in Example 11, using 2-(2-hydroxyethyl)piperidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.46(d, J=8Hz, 1H), 7.16-7.24(m, 2H), 7.11(ddd, J=8, 7, 1Hz, 1H), 6.84(s, 2H), 6.00-6.21(br, 1H), 5.08(s, 1H), 4.51-4.62(m, 1H), 3.57-3.66(m, 1H), 3.48-3.18(m, 3H), 2.69-2.88(m, 5H), 1.40-2.03(m, 8H), 1.38(s, 18H)
IR(cm^{-1}) 3640, 3320, 2950, 2870, 1640, 1530, 1440, 1275, 1230, 1175, 755

Example 182

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-2-(2-acetoxyethyl)piperidine

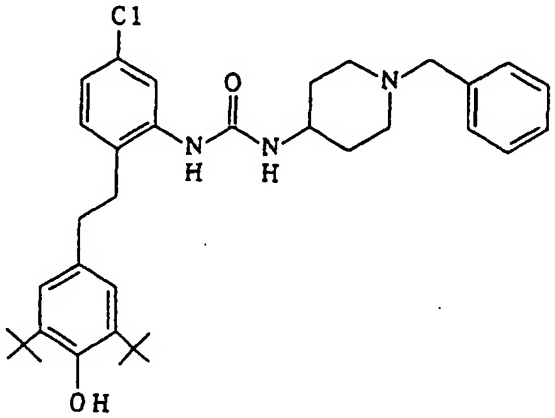


The title compound was prepared in a similar manner to that mentioned in Example 11, using 2-(2-acetoxyethyl)piperidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.49(d, J=8Hz, 1H), 7.17-7.23(m, 2H), 7.09(d, J=7Hz, 1H), 6.84(s, 2H), 5.84(s, 1H), 5.08(s, 1H), 4.33-4.43(m, 1H), 4.00-4.16(m, 2H), 3.41-3.51(m, 1H), 2.76-2.90(m, 5H), 2.00-2.12(m, 1H), 1.97(s, 3H), 1.74-1.85(m, 1H), 1.38-1.72(m, 6H), 1.38(s, 18H)
IR(cm^{-1}) 3640, 3425, 2960, 2870, 1740, 1640, 1520, 1435, 1370, 1235, 750

Example 183

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-5-chlorophenyl]N'-(1-benzyl-4-piperidyl)urea

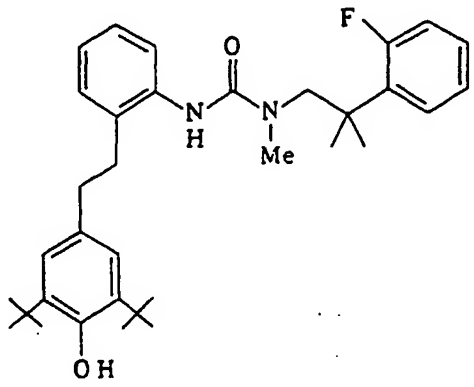


The title compound was prepared in a similar manner to that mentioned in Example 108, using 4-(2-amino-4-chlorophenethyl)-2,6-di-tert-butylphenol instead of 4-(2-amino-3,5-difluorophenethyl)-2,6-di-tert-butylphenol.
m.p. 155-156°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.41(s, 1H), 7.22-7.31(m, 5H), 7.08(s, 2H), 6.77(s, 2H), 5.22(s, 1H), 5.12(s, 1H), 4.20(d, J=8Hz, 1H), 3.45-3.65(m, 1H), 3.45(s, 2H), 2.75(s, 4H), 2.73-2.77(m, 2H), 2.04(t, J=11Hz, 2H), 1.85(d, J=11Hz, 2H), 1.38(s, 18H), 1.22-1.42(m, 2H)
IR(cm^{-1}) 3645, 3370, 1633, 1545, 1438, 1234, 699

Example 184

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-5-chlorophenyl]-N'-[2-(2-fluorophenyl)-2-methylpropyl]-N'-methylurea

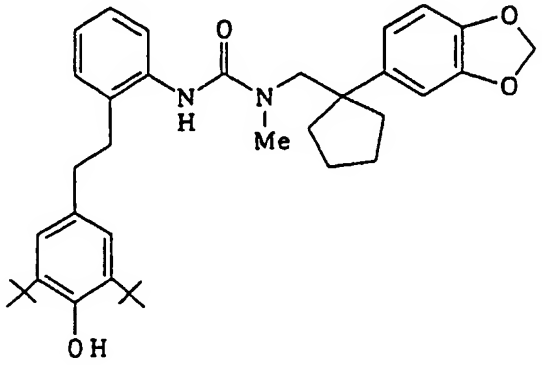


The title compound was prepared in a similar manner to that mentioned in Example 11, using 2-fluoro-β,β-dimethylphenethylamine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.53(d, J=8Hz, 1H), 7.17-7.28(m, 4H), 7.05-7.14(m, 2H), 6.94-7.03(m, 1H), 6.73(s, 2H), 5.49(s, 1H), 5.01(s, 1H), 3.70(s, 2H), 2.73-2.83(m, 4H), 2.21(s, 3H), 1.37(s, 6H), 1.29(s, 18H)
IR(cm^{-1}) 3640, 3430, 2965, 1660, 1510, 1490, 1440, 1210, 760

Example 185

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-5-chlorophenyl]-N'-methyl-N'-[1-(3,4-methylenedioxyphenyl)cyclopentyl]methylurea

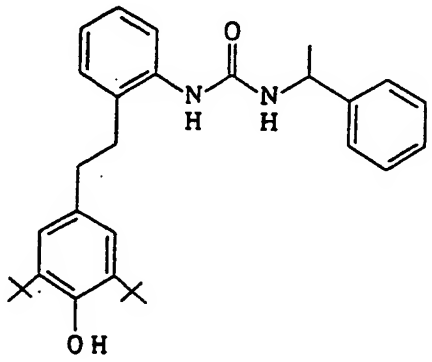


The title compound was prepared in a similar manner to that mentioned in Example 11, using 5-[1-(N-methylaminomethyl)cyclopentyl]-1,3-dioxaindane instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.45(d, J=7Hz, 1H), 7.16-7.24(m, 2H), 7.06-7.13(m, 1H), 6.78(s, 1H), 6.72(s, 4H), 5.92(s, 2H), 5.32(s, 1H), 5.03(s, 1H), 3.42(s, 2H), 2.73-2.82(s, 4H), 2.02(s, 3H), 2.58-2.98(m, 8H), 1.30(s, 18H)
IR(cm^{-1}) 3640, 3430, 2960, 1660, 1510, 1490, 1435, 1235, 1450, 760

Example 186

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-5-chlorophenyl]-N'-(α-methylbenzyl)urea

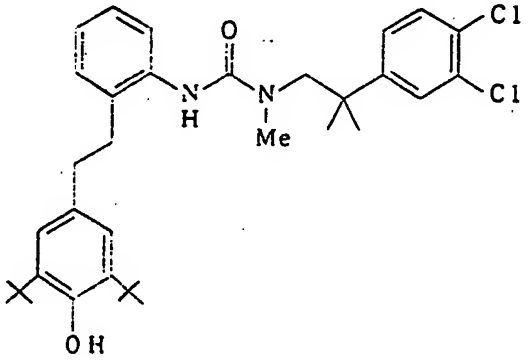


The title compound was prepared in a similar manner to that mentioned in Example 11, using α-methylbenzylamine instead of decylamine. m.p. 167-168°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.12-7.33(m, 9H), 6.77(s, 2H), 5.15(s, 1H), 5.09(s, 1H), 4.96(dq, J=7, 7Hz, 1H), 4.53(d, J=7Hz, 1H), 2.70-2.82(m, 4H), 1.40(d, J=7Hz, 3H), 1.37(s, 18H)
IR(cm^{-1}) 3625, 3320, 3275, 2960, 1630, 1565, 1435, 1235, 745, 700

Example 187

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-5-chlorophenyl]-N'-[2-(3,4-dichlorophenyl)-2-methylpropyl]-N'-methylurea



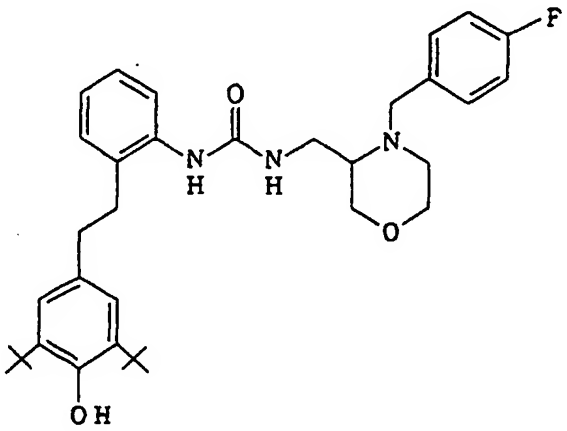
The title compound was prepared in a similar manner to that mentioned in Example 11, using N-methyl-3,4-dichloro-β,β-dimethylphenethylamine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.48(d, J=8Hz, 1H), 7.43(d, J=2Hz, 1H), 7.37(d, J=10Hz, 1H), 7.17-7.27(m, 3H), 7.09-7.15(m, 1H), 6.71(s, 2H), 5.38(s, 1H), 5.08(s, 1H), 3.48(s, 2H), 2.72-2.84(m, 4H), 2.13(s, 3H), 1.36(s, 6H), 1.29(s, 18H)

IR(cm^{-1}) 3640, 3430, 3330, 2970, 1660, 1515, 1480, 1450, 1440, 1310, 1250, 1030, 880, 760

Example 188

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-5-chlorophenyl]-N'-[4-(4-fluorobenzyl)-3-morpholinyl]methylurea



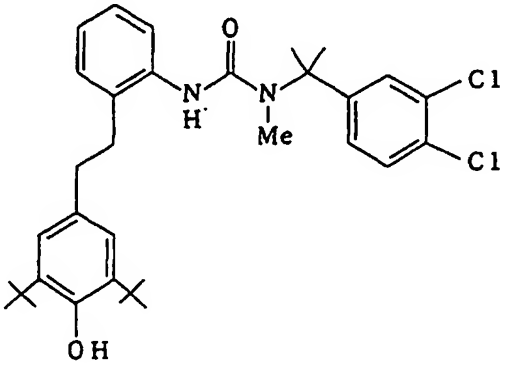
The title compound was prepared in a similar manner to that mentioned in Example 11, using 3-methylamino-4-(4-fluorobenzyl)morpholine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.19-7.37(m, 4H), 6.80-6.89(m, 4H), 6.76(s, 2H), 5.11(s, 1H), 5.05(s, 1H), 4.96(bs, 1H), 3.89(d, J=13Hz, 1H), 3.74(dd, J=12, 3Hz, 1H), 3.64(d, J=12Hz, 1H), 3.31-3.42(m, 4H), 3.03(d, J=13Hz, 1H), 2.70-

2.88(m, 4H), 2.48-2.56(m, 1H), 2.45(d, J=12Hz, 1H), 2.10(dt, J=11, 3Hz, 1H), 1.37(s, 18H)

Example 189

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-5-chlorophenyl]-N'-[2-(3,4-dichlorophenyl)-2-propyl]-N'-methylurea

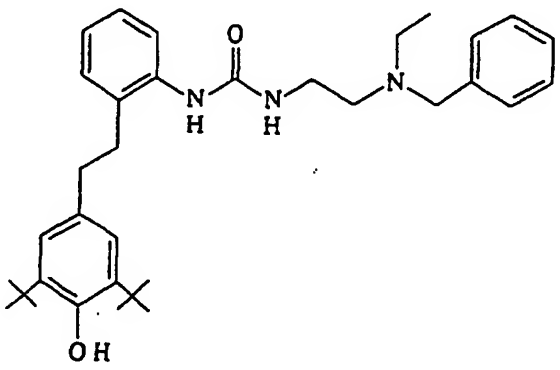


The title compound was prepared in a similar manner to that mentioned in Example 11, using 3,4-dichloroN,α,α-trimethylbenzylamine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.36-7.42(m, 2H), 7.24-7.29(m, 1H), 7.09-7.17(m, 3H), 7.02-7.07(m, 1H), 6.79(s, 2H), 5.52(s, 1H), 5.09(s, 1H), 2.81(s, 3H), 2.61-2.78(m, 4H), 1.63(s, 6H), 1.38(s, 18H)
IR(cm^{-1}) 3640, 3290, 2960, 2875, 1640, 1520, 1485, 1440, 1340, 1245, 1140, 1030, 755

Example 190

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-5-chlorophenyl]-N'-[2-(N-benzyl-N-ethylamino)ethyl]urea



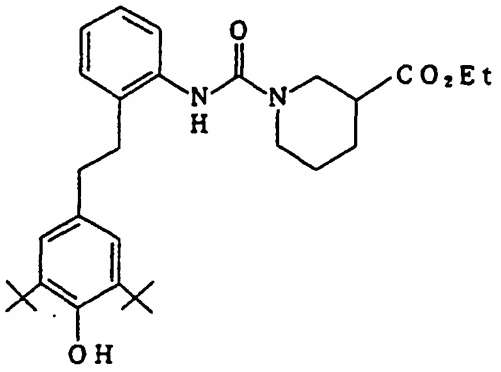
The title compound was prepared in a similar manner to that mentioned in Example 11, using N-benzyl-N-ethylethylenediamine instead of decylamine.
m.p. 132-133°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.16-7.36(m, 7H), 6.92-6.98(m, 2H), 6.79(s, 2H), 5.12(bs, 1H), 5.09(s, 1H), 5.00-5.05(m, 1H), 3.43(s, 2H), 3.21(td, J=6, 5Hz, 2H), 2.74-2.90(m, 4H), 2.46(t, J=6Hz, 2H), 2.37(q, J=7Hz, 2H), 1.38(s, 18H), 0.87(t, J=7Hz, 3H)

IR(cm^{-1}) 3650, 3340, 3280, 2960, 2810, 1640, 1585, 1560, 1440, 1235, 1150, 865, 745, 705

Example 191

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)phenyl]carbamoyl]-3-ethoxycarbonylpiperidine



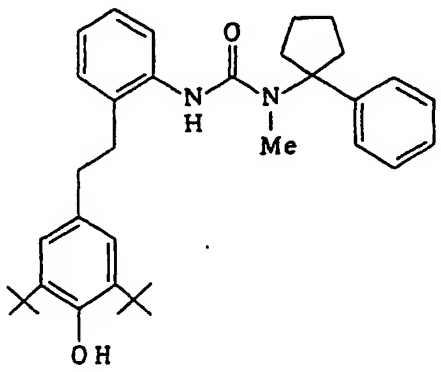
The title compound was prepared in a similar manner to that mentioned in Example 11, using 3-ethoxycarbonylpiperidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.53(d, J=8Hz, 1H), 7.15-7.22(m, 2H), 7.04-7.09(m, 1H), 6.84(s, 2H), 6.30(s, 1H), 5.07(s, 1H), 4.06-4.15(m, 2H), 3.74-3.81(m, 1H), 3.30-3.42(m, 2H), 3.10-3.17(m, 1H), 2.78-2.92(m, 4H), 2.52-2.59(m, 1H), 1.83-2.00(m, 2H), 1.46-1.66(m, 2H), 1.38(s, 18H), 1.22(t, J=7Hz, 3H)

IR(cm^{-1}) 3425, 2945, 2870, 1725, 1650, 1595, 1530, 1450, 1375, 1300, 1210, 1030, 885, 760

Example 192

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-5-chlorophenyl]-N'-(1-phenylcyclopentyl)-N'-methylurea



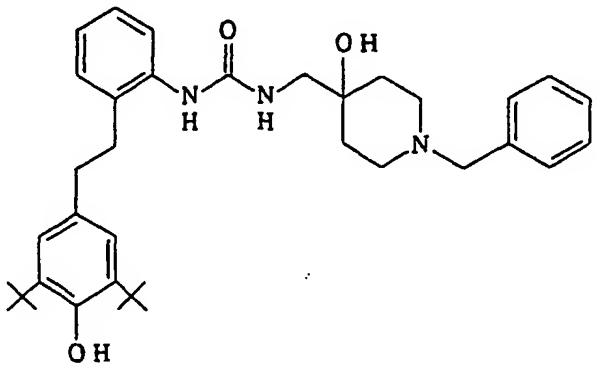
The title compound was prepared in a similar manner to that mentioned in Example 11, using N-methyl-1-phenyl-

cyclopentylamine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.47(d, J=8Hz, 1H), 7.33(dd, J=8, 1Hz, 1H), 7.08-7.18(m, 3H), 6.93-7.02(m, 3H), 6.78(s, 2H), 5.75(s, 1H), 5.07(s, 1H), 3.15(s, 3H), 2.57(t, J=8Hz, 2H), 2.23-2.39(m, 4H), 2.20(t, J=8Hz, 2H), 1.64-1.85(m, 4H), 1.42(s, 18H)
IR(cm^{-1}) 3630, 3410, 2950, 1640, 1520, 1440, 1345, 1230, 755, 700

Example 193

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-5-chlorophenyl]-N'-(1-benzyl-4-hydroxy-4-piperidyl)methylurea

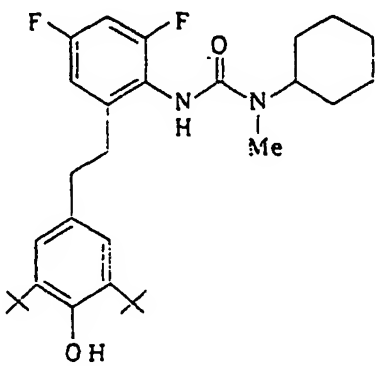


The title compound was prepared in a similar manner to that mentioned in Example 11, using 4-aminomethyl-1-benzyl-4-hydroxypiperidine instead of decylamine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.15-7.35(m, 9H), 6.76(s, 2H), 5.12(s, 1H), 5.08(bs, 1H), 4.56(t, J=5Hz, 1H), 3.51(s, 2H), 3.37(bs, 1H), 3.14(d, J=5Hz, 2H), 2.70-2.85(m, 4H), 2.50-2.60(m, 2H), 2.30-2.40(m, 2H), 1.45-1.60(m, 4H), 1.36(s, 18H)
IR(cm^{-1}) 3350, 2952, 1639, 1550, 1435, 1234, 741, 699

Example 194

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]-N'-cyclohexyl-N'-methylurea

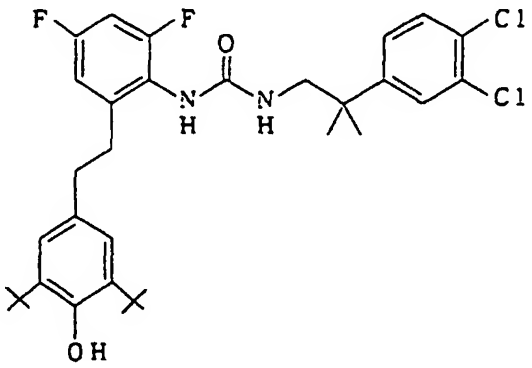


The title compound was prepared in a similar manner to that mentioned in Example 108, using N-methylcyclohexylamine instead of 4-amino-1-benzylpiperidine.

^{1}H-NMR(δ ppm, $CDCl_3$) 6.70-6.80(m, 2H), 6.79(s, 2H), 5.09(s, 1H), 4.98(bs, 1H), 4.00-4.10(m, 1H), 2.75-2.90(m, 4H), 2.60(s, 3H), 1.60-1.80(m, 4H), 1.20-1.50(m, 24H)
IR(cm^{-1}) 3630, 3420, 2930, 1639, 1499, 1435, 1317, 1237, 1119

Example 195

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]-N'-[2-(3,4-dichlorophenyl)-2-methylpropyl]urea

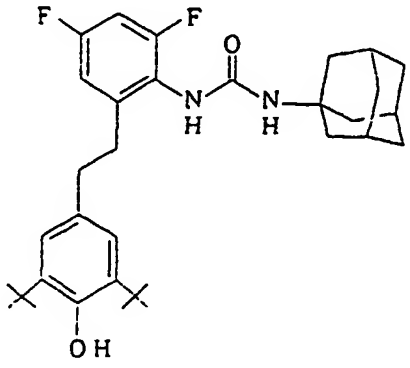


The title compound was prepared in a similar manner to that mentioned in Example 108, using 3,4-dichloro-β,β-dimethylphenethylamine instead of 4-amino-1-benzylpiperidine. m.p. 159-160°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.05-7.30(m, 3H), 6.65-6.78(m, 4H), 5.08-5.11(m, 1H), 4.27(bs, 1H), 3.72(bt, J=6Hz, 1H), 3.28-3.31(m, 2H), 2.65-2.80(m, 4H), 1.30-1.40(m, 18H), 1.20-1.30(m, 6H)
IR(cm^{-1}) 3640, 3310, 2958, 1638, 1566, 1436, 1235, 1118

Example 196

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]-N'-(1-adamantyl)urea

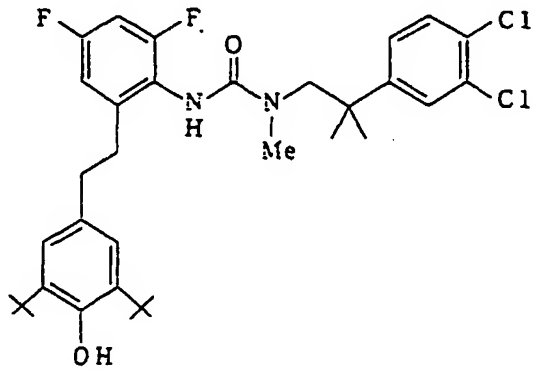


The title compound was prepared in a similar manner to that mentioned in Example 108, using 1-adamantanamine instead of 4-amino-1-benzylpiperidine.
m.p. 218-220°C

^{1}H-NMR(δ ppm, $CDCl_3$) 6.81(s, 2H), 6.70-6.80(m, 2H), 5.12(s, 1H), 4.60(bs, 1H), 3.93(bs, 1H), 2.88(t, J=7Hz, 2H), 2.78(t, J=7Hz, 2H), 2.03(bs, 3H), 1.91(d, J=3Hz, 6H), 1.64(bs, 6H), 1.40(s, 18H)
IR(cm^{-1}) 3642, 3375, 2910, 1650, 1562, 1495, 1436, 1235, 1120

Example 197

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]-N'-[2-(3,4-dichlorophenyl)-2-methylpropyl]-N'-methylurea

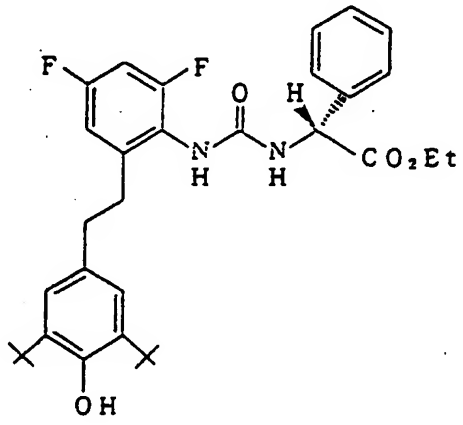


The title compound was prepared in a similar manner to that mentioned in Example 108, using N-methyl-3,4-dichloro-β,β-dimethylphenethylamine instead of 4-amino-1-benzylpiperidine. m.p. 145-147°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.15-7.40(m, 3H), 6.65-6.80(m, 4H), 5.04-5.06(m, 1H), 4.70-4.73(m, 1H), 3.46-3.49(m, 2H), 2.75-2.85(m, 4H), 2.20-2.24(m, 3H), 1.30-1.34(m, 24H)
IR(cm^{-1}) 3572, 3420, 2954, 1665, 1505, 1434, 1120

Example 198

(R)-N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]-N'-(α-ethoxycarbonylbenzyl)urea

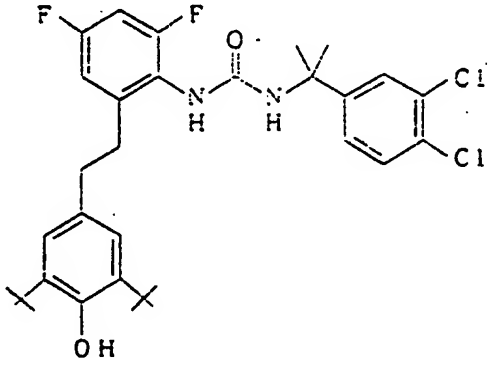


The title compound was prepared in a similar manner to that mentioned in Example 108, using (R)-α-phenylglycine ethyl ester instead of 4-amino-1-benzylpiperidine. m.p. 162-164°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.26-7.32(m, 5H), 6.73-6.80(m, 4H), 5.45(d, J=7Hz, 1H), 5.22(bd, J=7Hz, 1H), 5.12(s, 1H), 4.68(bs, 1H), 4.08-4.20(m, 2H), 2.72-2.89(m, 4H), 1.37(s, 18H), 1.18(t, J=7Hz, 3H)
IR(cm^{-1}) 3640, 3350, 2956, 1737, 1641, 1561, 1438, 1122

Example 199

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]-N'-[2-(3,4-dichlorophenyl)-2-propyl]urea

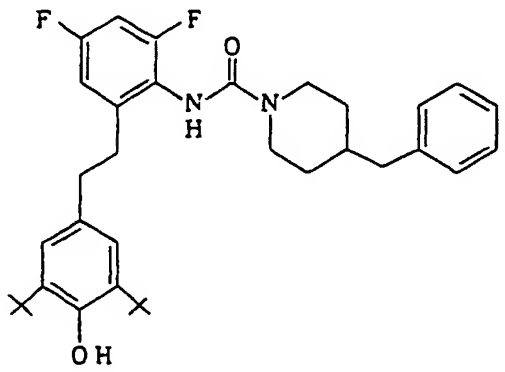


The title compound was prepared in a similar manner to that mentioned in Example 108, using 3,4-dichloro-α,α-dimethylbenzylamine instead of 4-amino-1-benzylpiperidine. m.p. 224-226°C

^{1}H-NMR(δ ppm, $CDCl_3$) 7.42(d, J=2Hz, 1H), 7.31(d, J=9Hz, 1H), 7.18(dd, J=9, 2Hz, 1H), 6.75-6.80(m, 4H), 5.13(s, 1H), 4.62(bs, 1H), 4.53(bs, 1H), 2.56(t, J=7Hz, 2H), 2.77(t, J=7Hz, 2H), 1.57(s, 6H), 1.40(s, 18H)
IR(cm^{-1}) 3634, 3354, 2954, 1649, 1562, 1435, 1277, 1238, 1122

Example 200

1-[N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]carbamoyl]-4-benzylpiperidine

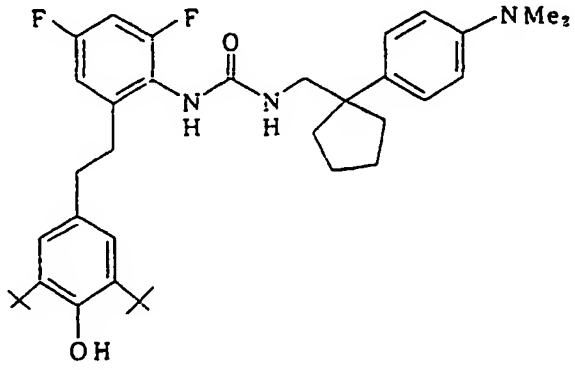


The title compound was prepared in a similar manner to that mentioned in Example 108, using 4-benzylpiperidine instead of 4-amino-1-benzylpiperidine.

^{1}H-NMR(δ ppm, $CDCl_3$) 7.25-7.31(m, 2H), 7.20(t, J=7Hz, 1H), 7.12(d, J=7Hz, 2H), 6.71-6.80(m, 2H), 6.75(s, 2H), 5.09(s, 1H), 4.96(s, 1H), 3.73(bd, J=13Hz, 2H), 2.78-2.85(m, 4H), 2.67(t, J=12Hz, 2H), 2.53(d, J=7Hz, 2H), 1.58-1.71(m, 3H), 1.36(s, 18H), 1.12-1.22(m, 2H)
IR(cm^{-1}) 3636, 3418, 3026, 1627, 1499, 1435, 1235, 1120, 789, 748, 700

Example 201

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]-N'-[1-(4-dimethylaminophenyl)cyclopentyl]methylurea



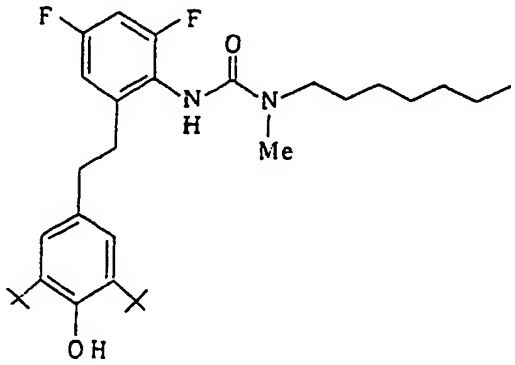
The title compound was prepared in a similar manner to that mentioned in Example 108, using 4-[(1-aminomethyl)-1-cyclopentyl]-N,N-dimethylaniline instead of 4-amino-1-benzylpiperidine. m.p. 165-166°C

^{1}H-NMR(δ ppm, $CDCl_3$) 6.92(d, J=9Hz, 2H), 6.75(s, 2H), 6.68-6.76(m, 2H), 6.54(d, J=9Hz, 2H), 5.08(s, 1H), 4.59(s, 1H), 3.82(bs, 1H), 3.19(d, J=6Hz, 2H), 2.89(s, 6H), 2.76(t, J=7Hz, 2H), 2.67(t, J=7Hz, 2H), 1.67-1.90(m, 8H), 1.37(s, 18H)

IR(cm^{-1}) 3674, 3250, 1615, 1520, 1435, 1233, 1121

Example 202

N-[2-(3,5-di-tert-butyl-4-hydroxyphenethyl)-4,6-difluorophenyl]-N'-heptyl-N'-methylurea



The title compound was prepared in a similar manner to that mentioned in Example 108, using N-methylheptylamine instead of 4-amino-1-benzylpiperidine.

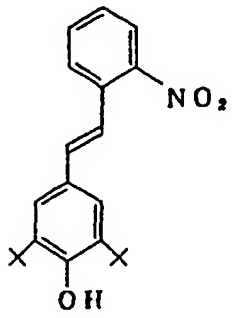
^{1}H-NMR(δ ppm, $CDCl_3$) 6.70-6.80(m, 2H), 6.77(s, 2H), 5.10(s, 1H), 4.96(s, 1H), 3.21(t, J=8Hz, 2H), 2.75-2.86(m, 4H), 2.75(s, 3H), 1.42-1.56(m, 2H), 1.37(s, 18H), 1.20-1.35(m, 8H), 0.87(t, J=7Hz, 3H)
IR(cm^{-1}) 3640, 3300, 1638, 1503, 1435, 1236, 1120

The preparation of the compound of formula (II) used in each of the above examples is illustrated by the following reference examples.

Reference Example 1

4-(2-Aminophenethyl)-2,6-di-tert-butylphenol

(1) 2,6-di-tert-Butyl-4-(2-nitrostyryl)phenol

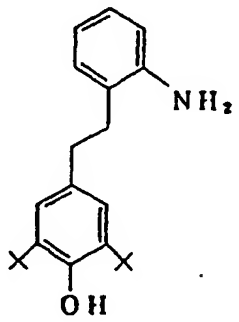


To a solution of 3,5-di-tert-butyl-4-hydroxybenzaldehyde (8.09 g, 34.5 mmol) and 2-nitrophenylacetic acid (9.40 g,

51.9 mmol) in xylene (60 ml) was added piperidine (0.3 ml) and the mixture was heated under reflux for 26 hrs while removing water producing with the progress of reaction. After allowing to stand overnight, hexane was added to afford as crystals 2,6-di-tert-butyl-4-(2-nitrostyryl)phenol (7.67 g, 62.9%).

^{1}H-NMR (δ ppm, $CDCl_3$) 7.94(dd, J=8, 1Hz, 1H), 7.76(d, J=8Hz, 1H), 7.57(dd, J=8, 8Hz, 1H), 7.44(d, J=16Hz, 1H), 7.33-7.37(m, 3H), 7.07(d, J=16Hz, 1H), 5.38(s, 1H), 1.48(s, 18H)

(2) 4-(2-Aminophenethyl)-2,6-di-tert-butylphenol

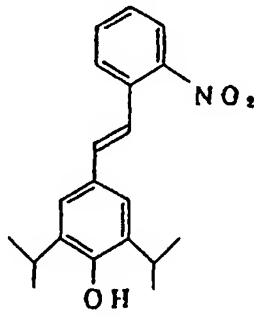


To a suspension of 2,6-di-tert-butyl-4-(2-nitrostyryl)phenol (16.4 g, 23.3 mmol) in ethanol (150 ml) was added a catalytic amount of 10% palladium carbon and the suspension was subjected to catalytic reduction at room temperature at 1-2.5 atms for 8 hrs and at 40°C for 3 hrs. After filtering the catalyst, distilling off the solvent gave 4-(2-aminophenethyl)-2,6-di-tert-butylphenol (15.1 g, 100%) as a viscous oil.

^{1}H-NMR (δ ppm, $CDCl_3$) 7.02-7.07(m, 2H), 6.94(s, 2H), 6.74-6.78(m, 1H), 6.67(d, J=8Hz, 1H), 5.06(s, 1H), 3.3-3.7(bs, 2H), 2.73-2.87(m, 4H), 1.41(s, 18H)

Reference Example 2

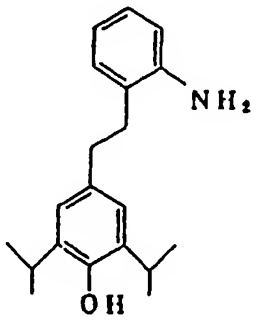
(1) 2,6-Diisopropyl-4-(2-nitrostyryl)phenol



To a solution of 3,5-diisopropyl-4-hydroxybenzaldehyde (0.95 g, 4.6 mmol) and 2-nitrophenyl acetic acid (1.1 g, 6.2 mmol) in xylene (10 ml) was added piperidine (0.05 ml) and the mixture was heated under reflux for 8 hrs while removing water producing with the progress of reaction. After distilling off the solvent followed by purification of the residue by a silica gel column chromatography, recrystallization from hexane gave 2,6-diisopropyl-4-(2-nitrostyryl)phenol (1.3 g, 87%) as crystals.

^{1}H-NMR (δ ppm, $CDCl_3$) 7.93-7.95(m, 1H), 7.75-7.77(m, 1H), 7.55-7.57(m, 1H), 7.45(d, J=16Hz, 1H), 7.34-7.38(m, 1H), 7.24(s, 2H), 7.07(d, J=16Hz, 1H), 4.95(s, 1H), 3.12-3.22(m, 2H), 1.32(s, 6H), 1.30(s, 6H)

(2) 4-(2-Aminophenethyl)-2,6-diisopropylphenol

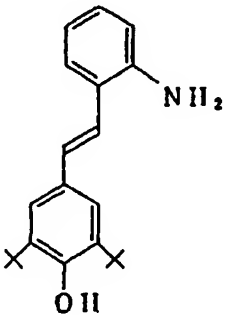


To a suspension of 2,6-diisopropyl-4-(2-nitrostyryl)phenol (1.3 g, 4.0 mmol) in ethanol (20 ml) was added a catalytic amount of 10% palladium carbon and the suspension was subjected to catalytic reduction at 1-2.5 atms at room temperature for 7 hrs. After filtering the catalyst, distilling off the solvent gave 4-(2-aminophenethyl)-2,6-diisopropylphenol (1.0 g, 84%) as a viscous oil.

^{1}H-NMR (δ ppm, $CDCl_3$) 7.02-7.06(m, 2H), 6.83(s, 2H), 6.70-6.77(m, 1H), 6.65(d, J=7Hz, 1H), 4.67(s, 1H), 3.43(bs, 2H), 3.08-3.18(m, 2H), 2.73-2.87(m, 4H), 1.24(s, 6H), 1.22(s, 6H)

Reference Example 3

4-(2-Aminostyryl)-2,6-di-tert-butylphenol



To a solution of 2,6-di-tert-butyl-4-(2-nitrostyryl)phenol (1.1 g, 3.1 mmol) in methanol (15 ml) was added water (4 ml), conc. hydrochloric acid (0.2 ml) and iron powder (1.7 g, 30 mmol) and the mixture was heated under reflux for 5 hrs. After filtration, followed by extraction with ethyl acetate and water, the extract was washed with water, dried over $MgSO_4$ and concentrated. Purification of the residue by a silica gel column chromatography followed by recrystallization from hexane afforded 4-(2-aminostyryl)-2,6-di-tert-butylphenol (0.70 g, 70%).

^{1}H-NMR (δ ppm, $CDCl_3$) 7.36-7.38(m, 1H), 7.34(s, 2H), 7.06-7.10(m, 1H), 6.91-7.10(m, 2H), 6.78-6.82(m, 1H), 6.70-6.72(m, 1H), 5.29(s, 1H), 3.79(s, 2H), 1.47(s, 18H)

Pharmacological Test

1. ACAT inhibitory activity

The enzyme preparation, ACAT was prepared from liver microsme fractions of male rabbits according to the method of E. E. Largis et al. (Journal of Lipid Research, Vol. 30, pages 681-690, 1989). The activity was calculated by assaying the amount of the labelled cholesteryl esters formed from [1-^{14}C]oleoyl-CoA and endogenous cholesterol according to the method of Kazuichi NATORI et al. (Japan J. Pharmacol., Vol. 42, pages 517-523, 1986).

The result is shown in Table 1, in which percent inhibition of the formation of the labelled cholesteryl esters with a compound added at 10^{-7}M is indicated as index for the ACAT inhibitory activity.

The data reveals that the compounds of the invention have a superior ACAT inhibitory activity.

2. Antioxidative activity

Human LDL was incubated in the presence of cupric sulfate (5×10^{-6}M) and in the presence or absence of a compound (10^{-5}M) for 5 hrs. After the incubation, the peroxidation of low-density lipoproteins (LDL) is evaluated by the formation of malondialdehyde (MDA), which is a sort of lipid peroxides according to the method of Simon J. T. Mao et al. (J. Med. Chem., Vol. 34, pages 298-302, 1991). Activity of the compound is shown by percent inhibition of the MDA formation as compared with control. The result is shown in Table 1. The data indicates that the compounds of the invention significantly lower the formation of the lipid peroxide (MDA). 3. Cholesterol-lowering activity

Sprague-Dawley male rats were given a powdery feed containing 1% cholesterol and 0.5% cholic acid in an amount of 15 g per day per animal for 3 days to produce hypercholesteremic rats. Four days later, a compound suspended in 0.5% methylcellulose was administered orally at a dose of 30 mg/kg. Blood was drawn prior to and 5 hrs after the administration of the compound, for which the plasma cholesterol level was measured using a commercially available assay kit (Cholesterol E Test Wako, Wako Junyaku K.K.). The result is shown in Table 2.

The data shows that the compounds of the invention significantly reduce blood cholesterol level.

Table 1

Compounds of Example	ACAT Inhibition (%)	Antioxidant Activity (%)
1	83	94
4	95	98
5	89	100
6	99	98
12	91	94
13	90	92
14	93	98
15	76	99
16	93	95
17	92	99
18	97	97

19	100	94
29	99	95
30	84	92
35	82	94
38	71	94
39	88	87
40	96	98
41	97	99
42	95	97
43	99	99
44	90	94
50	88	90
52	97	94
57	89	95
69	96	95
72	97	97
74	96	95
75	88	95
76	98	96
77	96	95
80	92	96
83	96	96
85	97	94
90	92	93
92	99	96
97	89	96

99	100	95
108	97	93
114	82	98
115	87	98
117	91	97
124	81	95
130	99	95
140	96	
141	86	
146	85	
155	94	
159	97	
163	81	
165	99	
166	100	
167	100	
168	93	
173	95	
177	98	
183	91	

Table 2

Compound of Example	Percent Reduction of Cholesterol (%)
35	48.4
83	44.6
92	79.9
105	45.9
108	71.8
130	71.5

The pharmaceutical preparations comprising the compounds of the invention are prepared by conventional method in accordance with the following formulations.

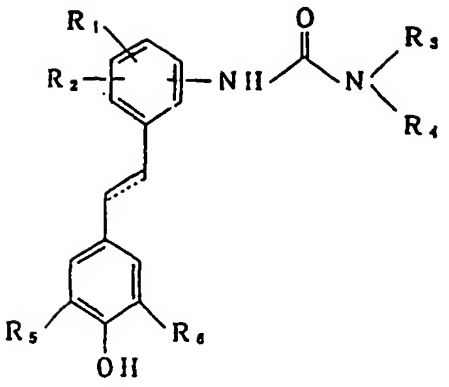
Tablets (per tablet)	
Compound of Example 6	50 mg
Hydroxypropylcellulose	2 mg
Corn starch	10 mg
Lactose	100 mg
Magnesium stearate	3 mg
Talc	3 mg

Capsules (per capsule)	
Compound of Example 17	200 mg
Starch	8 mg
Microcrystalline cellulose	23 mg
Talc	8 mg
Magnesium stearate	5 mg

Granules (per divided packet)	
Compound of Example 41	1 mg
Lactose	99 mg
Corn starch	50 mg
Crystalline cellulose	50 mg
Hydroxypropylcellulose	10 mg
Ethanol	9 mg

Claims

1. A compound of formula (I) or a pharmaceutically acceptable salt thereof



(I)

in which:

R_1 and R_2, which may be the same or different, each represents

a hydrogen atom,
a halogen atom,
a straight or branched (C_1-C_6)alkyl group or
a straight or branched (C_1-C_6)alkoxy group,

R_3 and R_4, which may be the same or different, each represents

a hydrogen atom,

a straight or branched (C_1-C_{12})alkyl group,

a straight or branched (C_2-C_{20})alkenyl group,

a (C_1-C_6)alkoxy(C_1-C_6)alkyl group,

a (C_1-C_6)alkoxycarbonyl(C_1-C_9)alkyl group,

a benzyloxycarbonyl(C_1-C_6)alkyl group in which the alkyl moiety is optionally substituted by phenyl,

a N,N-di(C_1-C_6)alkylamino(C_1-C_6)alkyl group,

a N-(C_1-C_6)alkyl-N-benzylamino(C_1-C_6)alkyl group,

a (C_1-C_6)alkylthio(C_1-C_6)alkyl group,

an oxo(C_1-C_9)alkyl group,

a hydroxy(C_1-C_6)alkyl group,

a dihydroxy(C_1-C_6)alkyl group,

a cyclo(C_3-C_{15})alkyl group,

a cyclo(C_3-C_8)alkyl(C_1-C_6)alkyl group,

a dicyclo(C_3-C_9)alkyl(C_1-C_6)alkyl group,

a bicyclo(C_6-C_9)alkyl group,

a tricyclo(C_9-C_{12})alkyl group,
in which in all cases the cycloalkyl group or the cycloalkyl moiety is optionally substituted by one or two substituents selected from the group consisting of (C_1-C_6)alkyl, hydroxy, amino, acetoxy, acetamido, phenyl, benzyloxy, dimethylaminophenyl, and methylenedioxyphenyl, which may be further fused with a benzene ring,

an aryl group,

an aryl(C_1-C_6)alkyl group,

a diaryl(C_1-C_6)alkyl group,
in which in all cases the aryl group or the aryl moiety is optionally substituted by one, two or three substituents selected from the group consisting of (C_1-C_6)alkyl, (C_1-C_6)alkyloxy, halogen, nitro, hydroxy, amino, dimethylamino, methylenedioxy, and pyrrolidinyl,

a heterocyclic group or

a heterocyclic group attached to a (C_1-C_6)alkylene chain,
in which in all cases the heterocyclic group represents a saturated or unsaturated, 5 to 8 membered ring monocyclic or bicyclic, heterocyclic group containing 1 to 3 heteroatoms selected from the group consisting of S, O and N, and the heterocyclic group is optionally substituted by one or two substituents selected from the group consisting of acetyl, hydroxy, (C_1-C_9)alkyl, (C_1-C_9)alkyloxy, cyclo(C_3-C_8)alkyl, cyclo(C_3-C_8)alkyl(C_3-C_{10})alkyl, pyridyl(C_1-C_6)alkyl, phenyl, phenyl(C_1-C_6)alkyl, diphenyl(C_1-C_6)alkyl, and phenylpiperazinyl, the phenyl group or the phenyl moiety being optionally substituted by one or two substituents selected from the group consisting of halogen, hydroxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, cyano, diethylamino and trifluoromethyl, which may be further fused with a benzene ring,

and further R_3 and R_4, together with the nitrogen atom to which they are attached, may form a saturated or unsaturated heterocyclic group,
in which the heterocyclic group represents a 5 to 8 membered ring monocyclic or bicyclic, heterocyclic group or a group derived from a heterocyclic spiro compound, which may contain one or two heteroatoms selected from the group consisting of S, O or N, the heterocyclic group being optionally substituted by one or two substituents selected from the group consisting of (C_1-C_6)alkyl, hydroxy, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, acetoxy(C_1-C_6)alkyl, (C_1-C_9)alkylcarbonyl, (C_1-C_6)alkoxycarbonyl, amino, tosyl, phenyl, halogenophenyl, (C_1-C_6)alkoxyphenyl, phenyl(C_1-C_6)alkyl, benzyloxy, benzyloxy(C_1-C_6)alkyl, tolyl, xylyl, benzoyl, methylenedioxyphenyl(C_1-C_6)alkyl, pyridyl, pyridylcarbonyl, piperidyl, pyrrolidinyl(C_1-C_6)alkyl and pyrrolidinylcarbonyl(C_1-C_6)alkyl, which may be further fused with a benzene ring,
in which in all cases the alkyl and alkoxy moieties may be either straight or branched,

with the proviso that both R_3 and R_4 do not represent a hydrogen atom at the same time;

R_5 and R_6, which may be the same or different, each represents a straight or branched (C_1-C_6)alkyl group; and the line

represents -CH_2CH_2- or -CH=CH-.

2. A compound of claim 1 wherein R_3 and R_4, which may be the same or different, each represents

a hydrogen atom,
a straight or branched (C_1-C_{10})alkyl group,
a straight or branched (C_3-C_{17})alkenyl group,
a (C_1-C_4)alkoxy(C_1-C_4)alkyl group,
a (C_1-C_4)alkoxycarbonyl(C_1-C_4)alkyl group,
a benzyloxycarbonyl(C_1-C_4)alkyl group in which the alkyl moiety is optionally substituted by phenyl,

a (C_1-C_4)alkylthio(C_1-C_4)alkyl group, a cyclo(C_3-C_{12})alkyl group or a cyclo(C_5-C_7)alkyl(C_1-C_4)alkyl group in which the cycloalkyl group or the cycloalkyl moiety is optionally monosubstituted by a substituent selected from the group consisting of (C_1-C_4)alkyl, hydroxy, amino, acetoxy, acetamide, phenyl, benzyloxy, dimethylaminophenyl and methylenedioxyphenyl, or the cycloalkyl group or the cycloalkyl moiety is optionally fused with a benzene ring;

a dicyclohexyl(C_1-C_4)alkyl group, a bicyclooctyl group, an adamantyl group, a phenyl group optionally substituted by (C_1-C_4)alkyl or hexyloxy, a naphthyl group, an anthryl group,

a phenyl(C_1-C_4)alkyl group in which the phenyl moiety is optionally substituted by one or two substituents selected from the group consisting of (C_1-C_4)alkyl, (C_1-C_4)alkyloxy, halogen, nitro, hydroxy, amino, dimethylamino, methylenedioxy and pyrrolidinyl;

a diphenyl(C_1-C_4)alkyl group, a heterocyclic group or a heterocyclic group attached to a (C_1-C_4)alkylene chain in which the heterocyclic group represents a saturated or unsaturated, 5 or 6 membered ring monocyclic or bicyclic, heterocyclic group containing 1 or 2 nitrogen atoms and the heterocyclic group is optionally substituted by one or two substituents selected from the group consisting of acetyl, hydroxy, (C_1-C_6)alkyl, cyclohexyl, pyridyl(C_1-C_4)alkyl, phenyl(C_1-C_4)alkyl or diphenyl(C_1-C_4)alkyl in which the phenyl moiety is optionally substituted by one or two substituents selected from the group consisting of halogen, (C_1-C_4)alkyl, (C_1-C_4)alkoxy, cyano, diethylamino and trifluoromethyl, and phenylpiperazinyl, which may be further fused with a benzene ring;

and further R_3 and R_4, together with the nitrogen atom to which they are attached may form a saturated or unsaturated heterocyclic ring, in which the heterocyclic group represents a 5 to 7 membered ring monocyclic or bicyclic, heterocyclic group or a group derived from a heterocyclic spiro compound, which contain one or two nitrogen atoms, the heterocyclic group being optionally substituted by one or two substituents selected from the group consisting of (C_1-C_4)alkyl, hydroxy(C_1-C_4)alkyl, acetoxy(C_1-C_4)alkyl, (C_1-C_6)alkylcarbonyl, (C_1-C_4)alkoxycarbonyl, tosyl, phenyl, phenyl(C_1-C_4)alkyl, benzyloxy, benzyloxy(C_1-C_4)alkyl, benzoyl, methylenedioxyphenyl(C_1-C_4)alkyl, pyridylcarbonyl, piperidyl and pyrrolidinylcarbonyl(C_1-C_4)alkyl.

3. A compound of claim 2 wherein R_3 and R_4, which may be the same or different, each represents a hydrogen atom, a straight or branched (C_1-C_7)alkyl group, a cyclo(C_4-C_8)alkyl group, a heterocyclic group or a heterocyclic group attached to a (C_1-C_4)alkylene chain in which the heterocyclic group represents a saturated or unsaturated, 5 or 6 membered ring monocyclic or bicyclic, heterocyclic group containing one nitrogen atom and the heterocyclic group is optionally substituted by one or two substituents selected from the group consisting of methyl, ethyl, cyclohexyl, pyridylmethyl, and phenyl(C_1-C_3)alkyl in which the phenyl moiety being optionally substituted by one or two substituents selected from the group consisting of halogen, methoxy, cyano, dimethylamino and trifluoromethyl, which may be further fused with a benzene ring.

4. A compound of claim 3 wherein R_3 and R_4, which may be the same or different, each represents a hydrogen atom, a straight or branched (C_1-C_4)alkyl group, cyclohexyl, cycloheptyl, pyrrolidinyl or piperidyl, the latter two heterocyclic groups being optionally substituted by one or two substituents selected from the group consisting of methyl, ethyl, cyclohexyl, pyridylmethyl, and phenyl(C_1-C_3)alkyl in which the phenyl moiety being optionally substituted by one or two substituents selected from the group consisting of halogen, methoxy, cyano, diethylamino and trifluoromethyl, which may be further fused with a benzene ring.

5. A compound of claim 2 wherein R_3 and R_4, together with the nitrogen atom to which they are attached, may form a saturated or unsaturated heterocyclic ring, in which the heterocyclic group represents a 5 or 6 membered ring monocyclic or bicyclic, heterocyclic group which contain one or two nitrogen atoms, the heterocyclic group being optionally substituted by one or two substituents selected from the group consisting of methyl, hydroxyethyl, acetoxyethyl, pentylcarbonyl, ethoxycarbonyl, tosyl, phenyl, benzyl, benzyloxy, benzyloxyethyl, benzoyl, methylenedioxybenzyl, pyridylcarbonyl and piperidyl, which may be further fused with a benzene ring.

6. A compound of formula (I) or a pharmaceutically acceptable salt thereof as claimed in any of claims 1 to 5 for use in therapy.

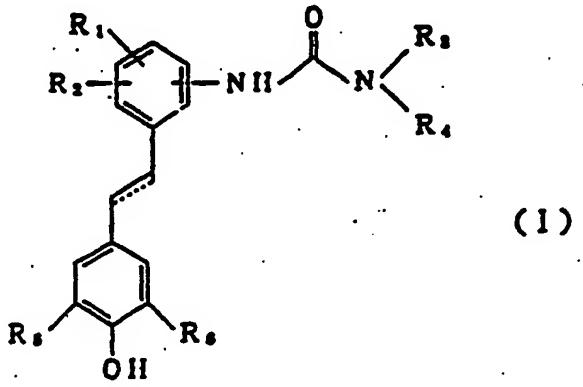
7. A compound as claimed in claim 6 for use in ACAT inhibition.

8. A pharmaceutical composition comprising as an active ingredient a compound of formula (I) or a pharmaceutically acceptable salt thereof as claimed in any of claims 1 to 5 and a pharmaceutically acceptable carrier and/or excipient.

9. Use of a compound of formula (I) or a pharmaceutically acceptable salt thereof as claimed in any of claims 1 to 5 in the manufacture of a medicament for the prophylaxis and treatment of hypercholesterolemia and atherosclerosis.

Patentansprüche

1. Verbindung der Formel (I) oder ein pharmazeutisch verträgliches Salz davon



(I)

worin:

R_1 und R_2, die gleich oder verschieden sein können, jeweils ein Wasserstoffatom,

ein Halogenatom,
eine gerade oder verzweigte (C_1-C_6)Alkylgruppe oder
eine gerade oder verzweigte (C_1-C_6)Alkoxygruppe wiedergeben,

R_3 und R_4, die gleich oder verschieden sein können, jeweils ein Wasserstoffatom,

eine gerade oder verzweigte (C_1-C_{12})Alkylgruppe,
eine gerade oder verzweigte (C_2-C_{20})Alkenylgruppe,
eine (C_1-C_6)Alkoxy(C_1-C_6)alkylgruppe,
eine (C_1-C_6)Alkoxycarbonyl(C_1-C_6)alkylgruppe,
eine Benzyloxycarbonyl(C_1-C_6)alkylgruppe, bei der die Alkylfunktionalität optional durch Phenyl substituiert ist,
eine N,N-di-(C_1-C_6)Alkylamino(C_1-C_6)alkylgruppe,
eine N-(C_1-C_6)Alkyl-N-benzylamino(C_1-C_6)alkylgruppe,
eine (C_1-C_6)Alkylthio(C_1-C_6)alkylgruppe,
eine Oxo(C_1-C_9)alkylgruppe,
eine Hydroxy(C_1-C_6)alkylgruppe,
eine Dihydroxy(C_1-C_6)alkylgruppe,
eine Cyclo(C_3-C_{15})alkylgruppe,
eine Cyclo(C_3-C_8)alkyl(C_1-C_6)alkylgruppe,
eine Dicyclo(C_3-C_9)alkyl(C_1-C_5)alkylgruppe,
eine Bicyclo(C_6-C_9)alkylgruppe,
eine Tricyclo(C_9-C_{12})alkylgruppe, bei der die Cycloalkylgruppe oder Cycloalkylfunktionalität in allen Fällen optional durch ein oder zwei aus der aus (C_1-C_6)Alkyl, Hydroxy, Amino, Acetoxy, Acetamido, Phenyl, Benzyloxy, Dimethylaminophenyl und Methylendioxyphenyl bestehenden Gruppe ausgewählten Substituenten substituiert sein können, die weiter mit einem Benzolring verbunden sein können,
eine Arylgruppe, eine Aryl(C_1-C_6)alkylgruppe,
eine Diaryl(C_1-C_6)alkylgruppe,
wobei die Arylgruppe oder die Arylfunktionalität in allen Fällen optional durch ein, zwei oder drei aus der aus (C_1-C_6)Alkyl, (C_1-C_6)Alkoxy, Halogen, Nitro, Hydroxy, Amino, Dimethylamino, Methylendioxy und Pyrrolidinyl bestehenden Gruppe ausgewählten Substituenten optional substituiert ist,
eine heterocyclische Gruppe oder eine an eine (C_1-C_6)Alkylenkette gebundene heterocyclische Gruppe,

wobei die heterocyclische Gruppe in allen Fällen eine gesättigte oder ungesättigte, 5- bis 8-gliederige, monocyclische oder bicyclische, heterocyclische Gruppe wiedergibt, die 1 bis 3 Heteroatome enthält, die aus der aus S, O und N bestehenden Gruppe ausgewählt sind, und die heterocyclische Gruppe optional durch einen oder zwei Substituenten substituiert ist, die aus der aus Acetyl, Hydroxy, (C_1-C_9)Alkyl, (C_1-C_9)Alkyloxy, Cyclo(C_3-C_8)alkyl, Cyclo(C_3-C_8)alkyl(C_3-C_{10})alkyl, Pyridyl(C_1-C_6)alkyl, Phenyl, Phenyl(C_1-C_6)alkyl, Diphenyl(C_1-C_6)alkyl und Phenylpiperazinyl bestehenden Gruppe ausgewählt sind, wobei die Phenylgruppe oder die Phenylfunktionalität optional durch ein oder zwei aus der aus Halogen, Hydroxy, (C_1-C_6)Alkyl, (C_1-C_5)Alkoxy, Cyano, Diethylamino und Triflourmethyl bestehenden Gruppe ausgewählt ist, die weiter mit einem Benzolring verbunden sein kann,

und R_3 und R_4 ferner, zusammen mit dem Stickstoffatom an das sie gebunden sind, eine gesättigte oder ungesättigte heterocyclische Gruppe bilden können,
wobei die heterocyclische Gruppe einen 5- bis achtgliederigen, monocyclischen oder bicyclischen Ring wiedergibt, eine heterocyclische Gruppe oder eine von einer heterocyclischen Spiro-Verbindung abgeleiteten Gruppe, die ein oder zwei aus der aus S, O oder N bestehenden Gruppe ausgewählte Heteroatome enthalten kann, die heterocyclische Gruppe optional durch ein oder zwei Substituenten substituiert ist, die aus der Gruppe bestehend aus (C_1-C_6)Alkyl, Hydroxy, Hydroxy(C_1-C_6)alkyl, (C_1-C_6)Alkoxy(C_1-C_6) alkyl, Acetoxy(C_1-C_6)alkyl, (C_1-C_9)Alkylcarbonyl, (C_1-C_6)Alkoxycarbonyl, Amino, Tosyl, Phenyl, Halogenphenyl, (C_1-C_6)Alkoxyphenyl, Phenyl(C_1-C_6)alkyl, Benzyloxy, Benzyloxy(C_1-C_6)alkyl, Tolyl, Xylyl, Benzoyl, Methylendioxyphenyl(C_1-C_6)alkyl, Pyridyl, Pyridylcarbonyl, Piperidyl, Pyrrolidinyl(C_1-C_6)alkyl und Pyrrolidinylcarbonyl(C_1-C_6)alkyl, die ferner mit einem Benzolring verbunden sein können,
wobei in allen Fällen die Alkyl- und Alkoxyfunktionalitäten entweder gerade oder verzweigt sein können, unter der Voraussetzung, daß beide, R_3 und R_4, nicht gleichzeitig ein Wasserstoffatom wiedergeben;

R_5 und R_6, die gleich oder verschieden sein können, jeweils eine gerade oder verzweigte (C_1-C_6)Alkylgruppe wiedergeben; und der Strich

$-CH_2-CH_2-$ oder CH=CH- wiedergibt.

2. Verbindung gemäß Anspruch 1, worin R_3 und R_4, die gleich oder verschieden sein können, jeweils ein Wasserstoffatom wiedergeben,

eine gerade oder verzweigte (C_1-C_{10})Alkylgruppe,
eine gerade oder verzweigte (C_3-C_{17})Alkenylgruppe,
eine (C_1-C_4)Alkoxy(C_1-C_4)alkylgruppe,
eine (C_1-C_4)Alkoxycarbonyl(C_1-C_4)alkylgruppe,
eine Benzyloxycarbonyl(C_1-C_4)alkylgruppe, in der die Alkylfunktionalität optional durch Phenyl substituiert ist,
eine (C_1-C_4)Alkylthio(C_1-C_4)alkylgruppe,
eine Cyclo(C_3-C_{12})alkylgruppe oder
eine Cyclo(C_5-C_7)alkyl(C_1-C_4)alkylgruppe, in der die Cycloalkylgruppe oder die Cycloalkylfunktionalität optional monosubstituiert ist durch einen Substituenten, ausgewählt aus der Gruppe bestehend aus (C_1-C_4)Alkyl, Hydroxy, Amino, Acetoxy, Acetamid, Phenyl, Benzyloxy, Dimethylaminophenyl und Methylendioxyphenyl, oder die Cycloalkylgruppe oder die Cycloalkylfunktionalität optional mit einem Benzolring verbunden ist;
eine Dicyclohexyl(C_1-C_4)alkylgruppe, eine Bicyclooctylgruppe, eine Adamantylgruppe, eine Phenylgruppe, optional substituiert durch (C_1-C_4) Alkyl oder Hexyloxy,
eine Naphthylgruppe,
eine Anthrylgruppe,
eine Phenyl(C_1-C_4)alkylgruppe in der die Phenylfunktionalität optional durch ein oder zwei Substituenten substituiert ist, die aus der aus (C_1-C_4)Alkyl, (C_1-C_4)Alkoxy, Halogen, Nitro, Hydroxy, Amino, Dimethylamino, Methylendioxy und Pyrrolidinyl bestehenden Gruppe ausgewählt sind;
eine Diphenyl(C_1-C_4)alkylgruppe, eine heterocyclische Gruppe oder eine heterocyclische Gruppe die an eine (C_1-C_4)Alkylenkette gebunden ist, in der die heterocyclische Gruppe einen gesättigten oder ungesättigten, 5- oder 6-gliedrigen monocyclischen oder bicyclischen Ring wiedergibt, wobei die heterocyclische Gruppe 1 oder 2 Stickstoffatome enthält und die heterocyclische Gruppe optional durch ein oder zwei Substituenten substitu-

iert ist, die aus der aus Acetyl, Hydroxy, (C_1-C_6)Alkyl, Cyclohexyl, Pyrridyl(C_1-C_4)alkyl, Phenyl(C_1-C_4)alkyl oder Diphenyl(C_1-C_4)alkyl, ausgewählt sind, wobei die Phenylfunktionalität optional durch ein oder zwei Substituenten substituiert ist, die aus der aus Halogen(C_1-C_4)alkyl, (C_1-C_4)Alkoxy, Cyano, Diethylamino und Triflourmethyl und Phenylpiperazinyl bestehenden Gruppe ausgewählt sind, die ferner mit einem Benzolring verbunden sein kann;

und ferner R_3 und R_4, zusammen mit dem Stickstoffatom, an das sie gebunden sind, einen gesättigten oder ungesättigten heterocyclischen Ring bilden können, wobei die heterocyclische Gruppe einen 5- bis 7-gliedrigen, mono- oder bicyclischen Ring wiedergibt, eine heterocyclische Gruppe oder eine von einer heterocyclischen Spiro-Verbindung abgeleiteten Gruppe, die ein oder zwei Stickstoffatome enthält, wobei die heterocyclische Gruppe optional durch ein oder zwei Substituenten substituiert ist, die aus der aus (C_1-C_4)Alkyl, Hydroxy(C_1-C_4)alkyl, Acetoxy(C_1-C_4)alkyl, (C_1-C_6)Alkylcarbonyl, (C_1-C_4)Alkoxycarbonyl, Tosyl, Phenyl, Phenyl(C_1-C_4)alkyl, Benzyloxy, Benzyloxy(C_1-C_4)alkyl, Benzoyl, Methylendioxyphenyl(C_1-C_4)alkyl, Pyridylcarbonyl, Piperidyl und Pyrrolidinylcarbonyl-(C_1-C_4)alkyl bestehenden Gruppe ausgewählt sind.

3. Verbindung gemäß Anspruch 2, wobei R_3 und R_4, die gleich oder verschieden sein können, jeweils ein Wasserstoffatom wiedergeben, eine gerade oder verzweigte (C_1-C_7)Alkylgruppe, eine Cyclo(C_4-C_8)alkylgruppe, eine heterocyclische Gruppe oder eine an eine (C_1-C_4)Alkylenkette gebundene heterocyclische Gruppe, wobei die heterocyclische Gruppe einen gesättigten oder ungesättigten, 5- oder 6-gliedrigen, monocyclischen oder bicyclischen Ring wiedergibt, eine ein Stickstoffatom enthaltende heterocyclische Gruppe und die heterocyclische Gruppe optional mit einem oder zwei Substituenten substituiert ist, ausgewählt aus der Gruppe bestehend aus Methyl, Ethyl, Cyclohexyl, Pyridylmethyl und Phenyl(C_1-C_3)alkyl, wobei die Phenylfunktionalität optional durch ein oder zwei Substituenten substituiert ist, die aus der Gruppe bestehend aus Halogen, Methoxy, Cyano, Dimethylamino und Triflourmethyl besteht, die ferner mit einem Benzolring verbunden sein kann.

4. Verbindung gemäß Anspruch 3, wobei R_3 und R_4, die gleich oder verschieden sein können, jeweils ein Wassserstoffatom wiedergeben, eine gerade oder verzweigte (C_1-C_4)Alkylgruppe, Cyclohexyl, Cycloheptyl, Pyrrolidinyl oder Piperidyl, wobei die letztgenannten beiden heterocyclischen Gruppen optional mit einem oder zwei Substituenten substituiert sind, die aus der Gruppe bestehend aus Methyl, Ethyl, Cyclohexyl, Pyridylmethyl und Phenyl(C_1-C_3)alkyl ausgewählt sind, wobei die Phenylfunktionalität optional mit einem oder zwei Substituenten substituiert ist, ausgewählt aus der aus Halogen, Methoxy, Cyano, Diethylamino und Triflourmethyl besthenden Gruppe, die ferner mit einem Benzolring verbunden sein kann.

5. Verbindung gemäß Anspruch 2, wobei R_3 und R_4, zusammen mit dem Stickstoffatom, an das sie gebunden sind, einen gesättigten oder ungesättigten heterocyclischen Ring bilden können, wobei die heterocyclische Gruppe eine 5- oder 6-gliedrige, monocyclische oder bicyclische, heterocyclische Gruppe wiedergibt, die ein oder zwei Stickstoffatome enthält, wobei die heterocyclische Gruppe optional mit einem oder zwei Substituenten substituiert ist, die aus der Gruppe bestehend aus Methyl, Hydroxyethyl, Acetoxyethyl, Pentylcarbonyl, Ethoxycarbonyl, Tosyl, Phenyl, Benzyl, Benzyloxy, Benzyloxyethyl, Benzoyl, Methylendioxybenzyl, Pyridylcarbonyl und Piperidyl ausgewählt sind, wobei diese ferner mit einem Benzolring verbunden sein können.

6. Verbindung gemäß Formel (I) oder einem pharmazeutisch verträglichen Salz davon, wie in einem der Ansprüche 1 bis 5 beansprucht, zur Verwendung in der Therapie.

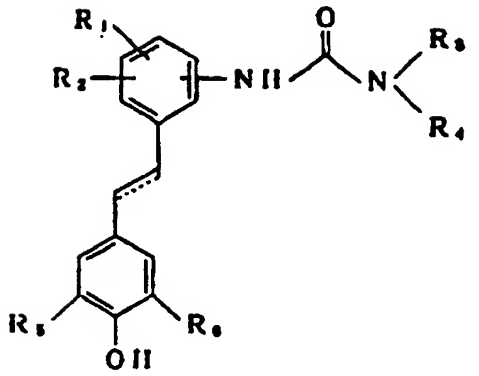
7. Verbindung, wie in Anspruch 6 beansprucht, zur Verwendung bei der ACAT-Inhibierung.

8. Pharmazeutische Zusammensetzung, als aktiven Bestandteil eine Verbindung der Formel (I) oder ein pharmazeutisch verträgliches Salz davon, wie in einem der Ansprüche 1 bis 5 beansprucht, und einen pharmazeutisch verträglichen Träger und/oder Hilfsstoff enthaltend.

9. Verwendung einer Verbindung der Formel (I) oder eines pharmazeutisch verträglichen Salzes davon, wie in einem der Ansprüche 1 bis 5 beansprucht, zur Herstellung eines Medikaments zur Prophylaxe und Behandlung von Hypercholesterolemie und Atherosklerose.

Revendications

1. Composé de la formule (I) ou un sel pharmaceutiquement acceptable de celui-ci :



(I)

dans laquelle :

R_1 et R_2, qui peuvent être identiques ou différents, représentent chacun

- un atome d'hydrogène,
- un atome d'halogène,
- un groupe (C_1-C_6)alcoyle droit ou ramifié, ou
- un groupe (C_1-C_6)alcoxy droit ou ramifié,

R_3 et R_4, qui peuvent être identiques ou différents, représentent chacun

- un atome d'hydrogène,
- un groupe (C_1-C_{12})alcoyle droit ou ramifié,
- un groupe (C_2-C_{20})alcényle droit ou ramifié,
- un groupe (C_1-C_6)alcoxy(C_1-C_6)alcoyle,
- un groupe (C_1-C_6)alcoxycarbonyl(C_1-C_9)alcoyle,
- un groupe benzyloxycarbonyl(C_1-C_6)alcoyle, dans lequel la fraction alcoyle est facultativement substituée par un phényle,
- un groupe N,N-di(C_1-C_6)alcoylamino(C_1-C_6)-alcoyle,
- un groupe N-(C_1-C_6)alcoyl-N-benzylamino(C_1-C_6)alcoyle,
- un groupe (C_1-C_6)alcoylthio(C_1-C_6)alcoyle,
- un groupe oxo(C_1-C_9)alcoyle,
- un groupe hydroxy(C_1-C_6)alcoyle,
- un groupe dihydroxy(C_1-C_6)alcoyle,
- un groupe cyclo(C_3-C_{15})alcoyle,
- un groupe cyclo(C_3-C_8)alcoyl(C_1-C_6)alcoyle,
- un groupe dicyclo(C_3-C_9)alcoyl(C_1-C_6)alcoyle,
- un groupe bicyclo(C_6-C_9)alcoyle,
- un groupe tricyclo(C_9-C_{12})alcoyle,

  dans lesquels, dans tous les cas, le groupe cycloalcoyle ou la fraction cycloalcoyle est facultativement substitué par un ou deux substituants sélectionnés dans le groupe comprenant un alcoyle à 1 à 6 atomes de carbone, hydroxy, amino, acétoxy, acétamido, phényle, benzyloxy, diméthylaminophényle et méthylènedioxyphényle, qui peuvent être en outre fusionnés avec un cycle benzénique,
- un groupe aryle,
- un groupe aryl(C_1-C_6)alcoyle,
- un groupe diaryl(C_1-C_6)alcoyle,

  dans lesquels, dans tous les cas, le groupe aryle ou la fraction aryle est facultativement substitué par un, deux ou trois substituants sélectionnés dans le groupe comprenant (C_1-C_6)alcoyle, (C_1-C_6)alcoyloxy, halogène, nitro, hydroxy, amino, diméthylamino, méthylènedioxy et pyrrolidinyle,
- un groupe hétérocyclique, ou
- un groupe hétérocyclique attaché à une chaîne (C_1-C_6)alcoylène,

dans lesquels, dans tous les cas, le groupe hétérocyclique représente un groupe hétérocyclique, monocyclique ou bicyclique, d'un cycle à 5 à 8 membres saturé ou insaturé, contenant 1 à 3 hétéroatomes choisis dans le groupe comprenant S, O et N, et le groupe hétérocyclique est facultativement substitué par un ou deux substituants choisis dans le groupe comprenant les suivants : acétyle, hydroxy, (C_1-C_9)alcoyle, (C_1-C_9)alcoyloxy, cyclo(C_3-C_8)alcoyle, cyclo(C_3-C_8)alcoyl(C_3-C_{10})alcoyle, pyridyl(C_1-C_6)alcoyle, phényle, phényl(C_1-C_6)alcoyle, diphényl(C_1-C_6)alcoyle et phénylpipérazinyle, le groupe phényle ou la fraction phényle étant facultativement substitué par un ou deux substituants choisis dans le groupe comprenant les suivants : halogène, hydroxy, (C_1-C_6)alcoyle, (C_1-C_6)alcoxy, cyano, diéthylamino et trifluorométhyle, qui peuvent en outre fusionner avec un cycle benzénique,

et en outre

R_3 et R_4, ensemble avec l'atome d'azote sur lequel ils sont attachés, peuvent former un groupe hétérocyclique saturé ou insaturé,

dans lequel le groupe hétérocyclique représente un groupe hétérocyclique, monocyclique ou bicyclique à cycle à 5 à 8 membres, ou un groupe dérivé d'un composé spiro hétérocyclique, qui peut contenir un ou deux hétéroatomes choisis dans le groupe comprenant S, O, et N, le groupe hétérocyclique étant facultativement substitué par un ou deux substituants choisis dans le groupe comprenant les suivants : (C_1-C_6)alcoyle, hydroxy, hydroxy(C_1-C_6)alcoyle, (C_1-C_6)alcoxy(C_1-C_6)alcoyle, acétoxy(C_1-C_6)alcoyle, (C_1-C_9)alcoylcarbonyle, (C_1-C_6)alcoxycarbonyle, amino, tosyle, phényle, halogénophényle, (C_1-C_6)alcoxyphényle, phényl(C_1-C_6)alcoyle, benzyloxy, benzyloxy(C_1-C_6)alcoyle, tolyle, xylyle, benzoyle, méthylènedioxyphényl(C_1-C_6)alcoyle, pyridyle, pyridylcarbonyle, pipéridyle, pyrrolidinyl(C_1-C_6)alcoyle et pyrrolidinylcarbonyl(C_1-C_6)alcoyle, qui peuvent être en outre fusionnés avec un cycle benzénique, dans lesquels, dans tous les cas, les fractions alcoyle et alcoxy peuvent être, soit droites, soit ramifiées,

sous réserve que R_3 et R_4 ne représentent pas tous deux un atome d'hydrogène en même temps ;

R_5 et R_6, qui peuvent être identiques ou différents, représentent chacun un groupe (C_1-C_6)alcoyle droit ou ramifié ; et la ligne

représente $-CH_2CH_2-$ ou $-CH=CH-$.

2. Composé selon la revendication 1, dans lequel R_3 et R_4, qui peuvent être identiques ou différents, représentent chacun :

- un atome d'hydrogène,
- un groupe (C_1-C_{10})alcoyle droit ou ramifié,
- un groupe (C_3-C_{17})alcényle droit ou ramifié,
- un groupe (C_1-C_4)alcoxy(C_1-C_4)alcoyle,
- un groupe (C_1-C_4)alcoxycarbonyl(C_1-C_4)alcoyle,
- un groupe benzyloxycarbonyl(C_1-C_4)alcoyle, où la fraction alcoyle est facultativement substituée par un phényle,
- un groupe (C_1-C_4)alcoylthio(C_1-C_4)-alcoyle,
- un groupe cyclo(C_3-C_{12})alcoyle, ou
- un groupe cyclo(C_5-C_7)alcoyl(C_1-C_4)alcoyle,

dans lesquels le groupe cycloalcoyle ou la fraction cycloalcoyle est facultativement monosubstitué par un substituant choisi dans le groupe comprenant les suivants : (C_1-C_4)alcoyle, hydroxy, amino, acétoxy, acétamide, phényle, benzyloxy, diméthylaminophényle et méthylènedioxyphényle, ou le groupe cycloalcoyle ou la fraction cycloalcoyle est facultativement fusionné avec un cycle benzénique ; un groupe dicyclohexyl(C_1-C_4)alcoyle, un groupe bicyclooctyle, un groupe adamantyle, un groupe phényle facultativement substitué par un (C_1-C_4)alcoyle ou hexyloxy, un groupe naphtyle, un groupe anthryle, un groupe phényl(C_1-C_4)alcoyle, dans lesquels la fraction phényle est facultativement substituée par un ou deux substituants choisis dans le groupe comprenant les suivants : (C_1-C_4)alcoyle, (C_1-C_4)alcoyloxy, halogène, nitro, hydroxy, amino, diméthylamino, méthylènedioxy et pyrrolidinyle ;
un groupe diphényl(C_1-C_4)alcoyle, un groupe hétérocyclique ou un groupe hétérocyclique attaché sur une chaîne (C_1-C_4)alcoylène, dans lesquels le groupe hétérocyclique représente un groupe hétérocyclique monocyclique ou

bicyclique à cycle à cinq à six éléments, saturé ou non saturé, contenant 1 ou 2 atomes d'azote, et le groupe hétérocyclique est facultativement substitué par un ou deux substituants choisis dans le groupe comprenant les suivants : acétyle, hydroxy, (C_1-C_6)alcoyle, cyclohexyle, pyridyl(C_1-C_4)alcoyle, phényl(C_1-C_4)alcoyle ou diphényl(C_1-C_4)alcoyle, dans lesquels la fraction phényle est facultativement substituée par un ou deux substituants choisis dans le groupe comprenant les suivants : halogène, (C_1-C_4)alcoyle, (C_1-C_4)alcoxy, cyano, diéthyalmino et trifluorométhyle, et phénylpipérazinyle, qui peuvent être en outre fusionnés avec un cycle benzénique ; et en outre R_3 et R_4, ensemble avec l'atome d'azote sur lequel ils sont attachés, peuvent former un cycle hétérocyclique saturé ou insaturé, dans lequel le groupe hétérocyclique représente un groupe hétérocyclique, monocyclique ou bicyclique, à cycle à 5 à 7 éléments, ou un groupe dérivé d'un composé spiro hétérocyclique, qui contient un ou deux atomes d'azote, le groupe hétérocyclique étant facultativement substitué par un ou deux substituants choisis dans le groupe comprenant les suivants : (C_1-C_4)alcoyle, hydroxy(C_1-C_4)alcoyle, acétoxy(C_1-C_4)-alcoyle, (C_1-C_4)alcoylcarbonyle, (C_1-C_4)-alcoxycarbonyle, tosyle, phényle, phényl(C_1-C_4)alcoyle, benzyloxy, benzyloxy(C_1-C_4)alcoyle, benzoyle, méthylènedioxyphényl(C_1-C_4)alcoyle, pyridylcarbonyle, pipéridyle et pyrrolidinylcarbonyl(C_1-C_4)alcoyle.

3. composé selon la revendication 2, dans lequel R_3 et R_4, qui peuvent être identiques ou différents, représentent chacun un atome d'hydrogène, un groupe (C_1-C_7)alcoyle droit ou ramifié, un groupe cyclo(C_4-C_8)alcoyle, un groupe hétérocyclique ou un groupe hétérocyclique attaché sur une chaîne (C_1-C_4)alkylène, dans lequels le groupe hétérocyclique représente un groupe hétérocyclique, monocyclique ou bicyclique, à cycle à cinq ou six éléments, saturé ou insaturé, contenant un atome d'azote, et le groupe hétérocyclique est facultativement substitué par un ou deux substituants choisis dans le groupe comprenant les suivants : méthyle, éthyle, cyclohexyle, pyridylméthyle, et phényl(C_1-C_3)alcoyle, la fraction phényle étant facultativement substituée par un ou deux substituants choisis dans le groupe comprenant les suivants : atome d'halogène, méthoxy, cyano, diméthylamino et trifluorométhyle, qui peuvent être en outre fusionnés avec un cycle benzénique.

4. Composé selon la revendication 3, dans lequel R_3 et R_4, qui peuvent être identiques ou différents, représentent chacun un atome d'hydrogène, un groupe (C_1-C_4)alcoyle droit ou ramifié, cyclohexyle, cycloheptyle, pyrrolidinyle ou pipéridyle, les deux derniers groupes hétérocycliques étant facultativement substitués par un ou deux substituants choisis dans le groupe comprenant les suivants : méthyle, éthyle, cyclohexyle, pyridylméthyle, et phényl(C_1-C_3)alcoyle, la fraction phényle étant facultativement substituée par un ou deux substituants choisis dans le groupe comprenant un atome d'halogène et les groupes suivants : méthoxy, cyano, diéthylamino et trifluorométhyle, qui peuvent être en outre fusionnés avec un cycle benzénique.

5. Composé selon la revendication 2, dans lequel R_3 et R_4, ensemble avec l'atome d'azote auquel ils sont attachés, peuvent former un cycle hétérocyclique saturé ou insaturé, dans lequel le groupe hétérocyclique représente un groupe hétérocyclique, monocyclique ou bicyclique, à cycle à cinq ou six éléments, qui contient un ou deux atones d'azote, le groupe hétérocyclique étant facultativement substitué par un ou deux substituants choisis dans le groupe comprenant les suivants : méthyle, hydroxyéthyle, acétoxyéthyle, pentylcarbonyle, éthoxycarbonyle, tosyle, phényle, benzyle, benzyloxy, benzyloxyéthyle, benzoyle, méthylènedioxybenzyle, pyridylcarbonyle et pipéridyle, qui peuvent être en outre fusionnés avec un cycle benzénique.

6. Composé de la formule (I) ou sel pharmaceutiquement acceptable de ce composé, selon l'une des revendications 1 à 5, pour utilisation en thérapie.

7. Composé selon la revendication 6, utilisé dans l'inhibition de ACAT.

8. Composition pharmaceutique comprenant, comme ingrédient actif, un composé de la formule (I) ou un sel pharmaceutiquement acceptable de celui-ci selon l'une des revendications 1 à 5, et un support et/ou un excipient pharmaceutiquement acceptable.

9. Utilisation d'un composé de la formule (I) ou d'un sel pharmaceutiquement acceptable de celui-ci selon l'une des revendications 1 à 5, dans la fabrication d'un médicament pour la prophylaxie et le traitement de l'hypercholestérolémie et de l'athérosclérose.